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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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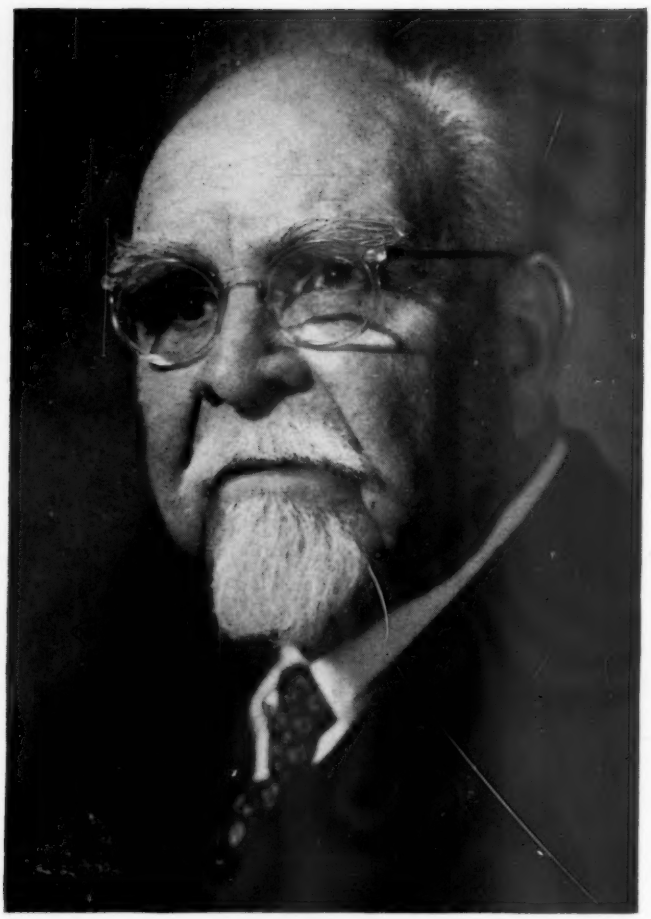

Rudolph Matas, M.D. (1860-), professor emeritus of surgery, School of Medicine, Tulane University, New Orleans, La.

SURGERY

VOL. 34 DECEMBER, 1953 No. 6

Original Communications

Society for Vascular Surgery

FOREWORD

GEZA DE TAKATS, M.D., CHICAGO, ILL.

THE history of surgery can be written in various ways. It is possible merely to record the development of ideas, impersonally, dispassionately, without reference to the lives of men who created them. It seems obvious, however, that the impetus which certain dominant figures have given to progress is only effective if their ideas and activities rapidly permeate contemporary thought and if these ideas then readily serve as building stones for the work of successive generations. Rudolph Matas' ingenuity, energy, and perseverance against many odds have created lines of thought in vascular surgery throughout the world; he may count hundreds of surgeons as being part of his school. His deep sense of historical development, his crystal-clear writing, and the recordings of vast clinical material from the Charity Hospital have made him a tower of wisdom and a lighthouse for future generations.

This issue of the JOURNAL contains the papers presented at the seventh annual meeting of the Society for Vascular Surgery. To our revered and beloved honorary member, who will recognize many of his early thoughts crystallized and implemented in these presentations, this issue is respectfully dedicated.

Introduction to the papers presented at the seventh annual meeting of the Society for Vascular Surgery, New York, N. Y., May 31, 1953.

RESPONSE TO FOREWORD

RUDOLPH MATAS, M.D., NEW ORLEANS, LA.

MY FIRST words on this occasion will be to acknowledge and thank you for the distinction you have conferred on me by dedicating the proceedings of your 1953 annual meeting to me. And I also wish to express the added pleasure it gives me to find this honor conferred on me between the presidencies of two fellow members and illustrious friends whose merits and friendship I appreciate so highly, Past President de Takats and President De Bakey. It will always remain one of my most agreeable reminiscences of this occasion that I have shared the pleasures of this dedication in company with these eminent and honored friends.

It also gives me great pleasure to learn that the President uses the gavel which the Society presented to me at Atlantic City, June 19, 1948, and which I had the gratification of placing in the custody of the Society at the same meeting. This historic gavel (made of Louisiana oak from the stairway of the old Charity Hospital in New Orleans, where I made my debut in vascular surgery) brings to my mind the very earliest years of the foundation of the Society (1946) and the birth of conservative vascular surgery (1888) and, seeing its use in the hands of the President, I am happy to recall the circumstances under which the first attempts of conservative vascular surgery became more or less historical. The word conservatism in this sense simply means the methods by which an aneurysm or other lesion in an artery can be eliminated or cured without injury to the blood-carrying function of the artery itself, and that is what is accomplished when, in curing an aneurysm, we substitute the suture, which preserves the continuity and lumen of the artery, for the ligature, which obliterates the lumen of the artery and arrests the circulation.

This dedication is particularly interesting and important to me because of its significance in recognizing the earliest record of conservatism in the treatment of aneurysms and the first challenge of conservative surgery in opposing the prevailing doctrine established from time immemorial that aneurysms could not be cured without arrest of the circulation in the artery of which they were a part. This was universally known and specifically stressed long after my graduation in 1880, although English-speaking surgeons then and even to the present day have failed to realize by whom this dictum was specifically emphasized, despite the fact that the European world recognized the greatness of the authority of its author, Antonio Scarpa (Pavia, 1804). His views remained universal even as late as 1913, when that eminent exponent of the cure of aneurysms by the method of ligation, Dr. Ballance of London, where John Hunter had so strongly advocated and emphasized the superiority

Read at the seventh annual meeting of the Society for Vascular Surgery, New York, N. Y., May 31, 1953.

of his ligature for the cure of aneurysms, reaffirmed the Scarpa dictum at the Congress of the International Society of Surgery held in London. It was at this Congress (1913) that I had an opportunity to report my personal experience in the conservative treatment of aneurysms as a challenge to the infallibility of Scarpa's dictum.

It was not until the appearance of Paul Moure's book (*Chirurgie vasculaire conservatrice,** the first systematic literature on the conservative treatment of arterial lesions, especially aneurysms, by substitution of the suture for the ligature) with its illustrations on the conservative treatment of aneurysms and vascular injuries, which was largely based on our correlated studies, that a conservative treatment of arterial injuries and aneurysms was brought to the attention of surgeons in Europe.

The challenge of my own publications and Moure's book were followed much later by the great and lasting emphasis of Leriche's authority and experience. In his admirable work (*Anévrismes artériels et fistules artérioveineuses*†), Leriche gives me credit for my own contributions and priority in conservative surgery as practiced clinically on human subjects in the treatment of aneurysms long before Carrel introduced or made known his admirable experimental work on the lower animals with a needle-and-thread technique which, admirable as it was, proved of comparatively little value when literally applied to the larger surgery of the human arteries.

MY PERSONAL EXPERIENCE

The honor that you have conferred on me by inviting me to accept this dedication also reminds me of the very earliest years of my own medical experience, when my early conception of the universally accepted and unquestioned Scarpa dictum was considerably upset by an experience I had in 1888 in operating on a young Negro who had developed a traumatic aneurysm in the left arm. This was caused by a number of fine shots which injured the brachial artery in many places and led to the formation of an aneurysm which continued to enlarge until it occupied one-half the arm from the armpit to the elbow. In this case the usual methods common at that time were carried out: elastic compression of the main artery and the aneurysm itself by the Reid-Clementi method, attempting in this way to arrest temporarily the circulation in the sac, hoping for coagulation in the sac and cure of the aneurysm; ligation of the artery at the upper pole of the sac; and, when, to our disappointment, pulsation in the aneurysm returned, application of a second ligature at the lower pole of the sac. Finally, as all these methods failed and we were faced with the possible loss of the arm, I determined to extirpate the aneurysmal sac. Accordingly, the operation was performed on April 6, 1888. However, an obstacle was found in carrying out this procedure because of the fact that it was impossible to extirpate the sac without also sacrificing the nerve supply of the arm, which would have resulted in complete paralysis of the arm. (The fear of limbs being left completely crippled or disabled made

*Paris, 1923, Masson & Cie.
†Paris, 1949, Masson & Cie.

amputation one of the obligate modes of treatment at that time in the case of certain aneurysms of the extremities.) In this quandary, wishing to avoid an amputation of the arm, I cleaned the sac of all clots and made every effort to find the orifices that were keeping the sac in active pulsation. In opening the sac I found a number of orifices from which blood was coming, evidently from collaterals, causing relapse of the aneurysm after ligation of the main artery that led to the sac. I searched for the bleeding orifices within the sac, probed them to determine their connection with the collaterals, and proceeded to suture the openings. I recalled the control of gunshot wounds of the intestines by suturing the orifices to prevent extravasation of intestinal contents, and it seemed a rational thing to control the hemorrhage by suturing the bleeding orifices. After suturing all the bleeding orifices within the sac (the wounded collaterals), I ordered the tourniquet released and found that the bleeding had all stopped. The sac became dry. Hemostasis was complete. In a short time the aneurysm dwindled to nothing as its blood supply was completely arrested, to my astonishment and great satisfaction. I then closed the wound, which healed, and the patient recovered with good use of the arm.

The success of this procedure was strange to me because I had never seen it performed. I had read of no instance in which bleeding had been stopped by suturing the intrasaccular sources of supply to the aneurysm after ligation of all the arterial parent trunks. This circumstance led me to see what my teachers and the current texts of the classic authors said about it. I was still a very young graduate in 1888, and spoke to all my colleagues at the time, Professor Richardson, Professor Logan, Professor Souchon, Professor Miles, and others, who had had the largest experience in arterial surgery, especially those who had served as Army surgeons of the Confederacy. Everywhere it seemed a novelty. In earlier days, when everything had failed to cure an aneurysm of the great arteries, the only recourse was to amputate; at least that was the general opinion, sustained by the great authority of such men as Percivall Pott, who advocated amputation in aneurysms of the extremities. No one used sutures for the control of hemorrhage, everyone ligated. And everyone was surprised that I had secured complete arrest of the aneurysm by simple intrasaccular sutures, apparently of collateral branches.

Upon further inquiry into the literature of the time, including the textbooks of Hunter, Ashurst, Bell, Ferguson, Pajet, and the classic French and German authors, I found that all concurred in the same opinion in advocating the classical methods of dealing with such complex situations. My procedure of intrasaccular suture of the bleeding orifices was so simple that I was surprised to find it had never been described or even mentioned. In reviewing the literature at that time I found that surgery of the blood vessels was considered the finest achievement of the surgery of the day, due to the danger of hemorrhage following the ligation of the great arteries, the innominate, the common carotid, the iliacs, the femorals, and the popliteals. Bleeding always appeared as an almost obligate sequel of ligation of the great arteries which, becoming inevitably septic, led to suppuration and then secondary hemorrhage

on detachment of the ligature which invariably occurred six or eight days after the operation. This was bad enough as a common occurrence of the peripheral arteries, but it was another matter when dealing with the aorta and its great visceral branches.

Throughout the texts, successful ligation of these arteries was considered an achievement of great merit. No one dreamed of purposely ligating the aorta, and the few cases reported (all fatal) were looked upon as phenomenal and largely adventurous procedures. Confirming this opinion, the leading surgeons of the world were distinguished by the number and success of the ligations they had performed. The surgeon who had the most experience in this field of surgery was Valentine Mott, who had ligated as many as 137 of the larger arteries. He practiced in New York and his universal fame was recognized throughout the world.

This continued to be the case until Lister taught us the one and only way of making the ligation of arteries less dangerous, by introducing asepsis and chemically sterilized catgut, which could be absorbed, preventing infection of wounds and ligatures. During the time I began practice, all methods were practically septic in New Orleans, except for a few like that of Schuppert (a pupil of Volkmann), who had introduced chemical disinfection and absorbable ligatures in New Orleans (1876 to 1878) by the use of solutions and sprays of carbolic acid. Much later, a few innovators substituted bichloride on the basis of Koch's researches, which endeavored to establish the superiority of bichloride as a germicide. These researches were in the eighties, seventy years ago.

However, apart from preventive asepsis and lack of control of infection in the treatment of aneurysms, one fact was slow in being recognized, that the dictum of Scarpa really could be challenged with apparent impunity, provided we could also prevent sepsis, and that an aneurysm could frequently be cured, after bleeding was controlled by constriction of the limb with an elastic bandage followed by opening the sac, clearing it of all clots, and suturing the orifices in the sac that were fed from the main or nutritive artery.

After my first experience in the operation which I subsequently called endoaneurysmorraphy (suture within the aneurysm), I had other experiences which encouraged me very much in the intrasaccular suture of arteries. A few months after my first operation, a young man from Central America, who had a traumatic aneurysm of the arm caused by shots, came to me. Upon operation I evacuated the sac and sutured the single large orifice of communication with the main artery visible within the sac, so that the aneurysm was cured and the lumen of the artery remained open. I continued to operate in this way, adding to the technique, so that I had three forms or types of operation, which I described as the obliterative, the restorative, and the reconstructive, in which I was able to deal with aneurysms from inside by means of sutures. Here it was that the suture replaced the ligature. Instead of performing the classical Hunterian operation, which consisted of ligating the main artery outside of the sac, I performed endoaneurysmorraphies.

Furthermore, later on, when I visited my former assistant, Dr. Warren Bickham, when he resided in New York (1902), we devised another method of utilizing sutures for the cure of arteriovenous aneurysms, restoring the patient's normal circulation by suturing the fistula that connected the artery and vein. The methods of technique which we recommended for the cure of arteriovenous aneurysms became well known in the surgical world. We cured a very large percentage of arteriovenous aneurysms by our methods, which were designated by several names, transvenous suture, obliteration of the fistula, and so forth. The details of most of these have been described in so many places, especially in my chapter in Keen's *Surgery,** that I will not burden this paper with details.

In the course of time, my practice in the treatment of aneurysms became quite large, as my own students and other surgeons continued to send me cases. The number of my operations accumulated until, at the time of my retirement from private practice, I had as part of my personal experience over 620 operations on the large arteries for aneurysms and other conditions, 519 operated by methods of ligation (including removable aluminum bands) and 101 by suture methods (including 98 endoaneurysmorraphies), and in all cases, all sutures and ligatures were buried in the tissues. In this we can see a decided contrast between my experience and experience in the days of Valentine Mott, whose total of 137 was the largest on record in civilian practice at that time. Also, there is a decided contrast in mortality between the pre-Listerian methods of Mott and mine under aseptic conditions. Changes in technique as well as aseptic methods made a very large difference in the direction of progress.

It was in this way that endoaneurysmorraphy, by either one of the three methods, the obliterative, restorative, or reconstructive, cured aneurysms with aseptic sutures (cut short and buried in the tissues) which closed all orifices in the sac that led to the main artery. By this procedure, all the circulation in the aneurysm was suppressed, and yet there was no encroachment upon the lumen of the main artery. It is in this way, unquestionably, that the mortality from this very serious affection of the arteries was conquered, since the introduction of aseptic surgery with aseptic and buried sutures made possible the development of conservative treatment in the cure of aneurysms of the great peripheral arteries.

ON THE VITAL IMPORTANCE OF OPEN THORACOTOMY AS A PREVENTIVE OF SURGICAL PNEUMOTHORAX

Alongside the great success of this method of dealing with the peripheral vessels, there still remained the great aneurysms of the central and visceral arteries, in which the anatomic conditions made them impossible of approach and cure by the methods of control that were common to the peripheral vessels. New methods had to be developed to deal with such arteries as the thoracic aorta and the abdominal aorta. There was an unsolved problem remaining

*Surgery of the Vascular System, vol. 5, chapt. LXX, Surgery, Its Principles and Practice, Philadelphia, 1914, W. B. Saunders Company.

which concerned all surgical manipulations of the aorta. Some means to enter the thorax safely had to be devised. Again I had occasion to participate at the very beginning of the solution of this problem by introducing the method of intralaryngeal insufflation,* in which I am an acknowledged pioneer. Now the surgery of the thorax presents an entirely different problem. Aneurysms of the aorta were unconquered, formidable, and intractable in the early years of my practice. They could not be cured by truly surgical methods until we discovered methods by which it was possible to maintain the supply of air in the lungs during operation. In this way it became possible to attack aneurysms of the aorta with some possibility of success. And now we have come to learn how to deal with this gravest of all forms of aneurysmal disease.

It was my good fortune to have been one of the pioneers in surgery of the aorta before my retirement (first successful ligation of the abdominal aorta, April 9, 1923), and I have been deeply concerned with the advances which have come up in the last ten years which have completely revolutionized the treatment of aortic aneurysms. It is only now that we have attained the supreme height of success in dealing with these formidable aneurysms by discovering the possibility of extirpating the aneurysms and transplanting whole segments of aorta and suturing them in place successfully, utilizing homologous grafts from man to man of segments successfully preserved indefinitely by the freeze-dried method recently perfected at Bethesda (Marrangoni and Ceccheni, 1951, Pate and Sawyer, 1953). This is entirely a new field for which the members of this Association have contributed the most advances in the world.

We must remember that, of all our successes, the absolute climax of success has not yet been obtained at the present time, but much progress has been accomplished, and the supreme height of conquest will not be long delayed. Just as the hitherto forbidding, unconquerable Mt. Everest has at last come to be subdued by the continued and persistent efforts of later and better-equipped and informed explorers, so aortic aneurysms, so long believed incurable, are at last being subdued and conquered by science and the master hand of surgery. The realization of this dream was considered utterly impossible in the almost immediate past, when the successful ligation of an aorta was looked upon by the surgical world as an almost universally fatal surgical procedure, and when the successful suture of wounded hearts and the extraction of foreign bodies from the heart chambers were regarded, and rightfully so, as magnificent and rare triumphs. And now, in the space of at most three years, the control, mastery, and replacement of injured and diseased aortas and the repair of congenitally malformed, traumatized, and condemned hearts have become so extraordinarily numerous and simplified in the hands of expert operators, that operations on the aorta and heart itself have become at this moment so banal and so successful that they are threatening to drop from their commanding rank in the modern hierachy of surgical attainment.

*History and Methods of Intra-laryngeal Insufflation for the Relief of Acute Surgical Pneumothorax, Tr. South. Surg. & Gynec. Assn. **12**: 52-82, 1899; J. A. M. A. **34**: 1468-1473, 1900.

While dealing with the triumphs of the needle and suture for the cure of arterial and arteriovenous aneurysms, which established a new chapter in the history of the surgical treatment of aneurysms, we should note that, in establishing the importance of the suture in opposition to the ligature, new methods of dealing with aneurysmal and cardiovalvular disease have gradually developed into a greatly expanded application of the suture as a vast contribution hitherto unsuspected in the cure of other numerous affections of the heart and great blood vessels.

It is fair to state that in the treatment of aneurysms alone (arterial and arteriovenous) the contrast between the success and simplicity of the suture methods over the classical ligatures has been particularly exhibited in the surgery of war, when lesions of the arteries and the creation of aneurysms is enormously increased, and in which arterial wounds constitute by far the most fatal consequences of war injuries.

While the advantages of the method of suturing arterial wounds and creating new methods of cure for the traumatic aneurysms of warfare had already been appreciated in World War I (as already demonstrated in our civilian practice), the benefits of suturing war wounds and curing war aneurysms were not really recognized until World War II, when the suture of war wounds and war aneurysms became so important that the military surgeons who directed the surgical treatment of the armed forces had to be trained in the special knowledge of a form of arterial surgery particularly applicable to the conditions of warfare. The application of these new developments in arterial surgery, as seen in its most recent and advanced phases in Korea, has so completely modernized the surgery of the blood vessels that the older teachings of fifteen or twenty years ago have become virtually historical, if not altogether obsolete. When we consider the great importance which was once attached to simple wounds of the heart, to foreign bodies in the heart, to other manifestations of traumatisms due to war injuries, and to other wounds and deformities of the heart and great arterial trunks, we cannot help but realize how relatively insignificant they all appear in the presence of the marvelous accomplishments of the present day.

The surgery of the great arteries of the heart, neck, thorax, and abdomen have compelled a complete revision on the part of students for a new surgical knowledge of the anatomy and, especially, the embryology of the great vessels that spring from the heart and neck. Techniques for these operations have led to changes in our armamentarium and acquisitions to our language so new in the nomenclature of cardiovascular surgery that they are not yet to be found in the very latest dictionaries. New instruments, each named for its inventor, include the rib raspatory, elevator, stripper, spreader; costotome, thoracoscope, thoracotome; artery clamps, forceps, tourniquets, probes, needles, and needle holders; cardiac holders, cardiac dilators, infundibular punches, mitral stenosis knives, guillotine knives, auricular appendage clamps, auricular wells; coarctation clamps, oxygenators, and many others which must be seen to be thoroughly appreciated. Reports of cardiovascular surgery speak

of the methods of "finger fracture" or "finger guillotine," of mitral, aortic, or pulmonary valvulotomy, valvuloplasty, valvular suspension, of commissurotomy, commissurorrhaphy, of a by-pass or shunt, of aortectomy, aortorrhaphy, and many others.

Needless to add, simply the names alone of these various operations and the techniques used have multiplied in such numbers that they constitute in themselves material for a new medical encyclopedia, and the names of the surgeons performing them would embrace the leading representatives of the whole surgical world, so great is the interest and enthusiasm with which this new line of surgical inventiveness is now being pursued.

Most notable among the earliest successes obtained was the successful treatment of congenital abnormalities which so often prove fatal at birth or, later on, bring the life of the infant or young child to a premature or early termination. Among the earliest of these great accomplishments in the relief of congenital vascular defects was the first conquest of a congenital defect known as the patent ductus arteriosus, an achievement long dreamed of, but regarded as only a medical exercise for the anatomic laboratory. The first hope held for its relief and cure came when Robert E. Gross, of Boston, performed the first successful ligation of the ductus arteriosus in a living human subject, in August, 1938, and in this way started a new surgery of this duct, which has brought back to life hundreds and thousands of infants in almost every great pediatric clinic in the world.

Following this first triumph came the discovery of an operation for the cure of congenital pulmonary stenosis and the tetralogy of Fallot. The symptom known popularly as "blue babies" (due to cyanosis of the face) has also passed away from the realm of infantile mortality in all its dangers and interference with the growth and health of the newborn child and has become one of the proudest possessions of vascular surgery, a great feat which, coming almost in immediate succession to advances in surgery of the ductus arteriosus, has left the name of Alfred Blalock indelibly imprinted in the history of modern surgery. Blue babies have been rescued from the ignorance and darkness of the past to a positive cure by the method first inaugurated by Blalock (Nov. 29, 1944) and now applicable in various ways in all the great clinics over the world with an enormous improvement in infantile mortality everywhere where skillful surgeons are capable and ready to apply successfully the Blalock operation or its modifications.*

The importance of diagnosing these conditions has elevated the merit of diagnosticians to a plane of distinction on a level with the merit displayed by surgeons in the operative technique for their relief, as is well exemplified by the splendid achievements of Dr. Helen Taussig, a member of Dr. Blalock's staff at The Johns Hopkins Hospital.

Continuing in the line of progress, we must refer to the realization of another conquest which had not been dreamed of in the past, and that is the

*As an illustration of the activity prevailing in his clinic at The Johns Hopkins Hospital, Dr. Blalock stated in a letter to Dr. Matas, dated June 30, 1952, that up to that time he had performed 1,155 operations for tetralogy of Fallot and over 60 on the pulmonic valve.

surgery for the cure of congenital defects of the aorta itself in the deformity known as coarctation, a veritable conquest, not only in the operative resources we now command for its relief, but also in the splendid accomplishments of the clinicians who have learned to make the early diagnosis, without which the defect would continue to progress to an early fatal termination.

Clarence Crafoord, of Stockholm, is credited with the first successful operation for coarctation (Oct. 19, 1944); almost coincidently, Alexander and Byron, of Ann Arbor, Mich., obtained an extraordinary success in suturing the aorta at the site of an excised section of a coarctation including an associated aneurysm (1944). Soon thereafter (1945) Robert Gross began an impressive series of operations for the relief of coarctation with or without aneurysm, and he is universally recognized as the first to replace the excised segment of aorta with an homologous graft (1949).

Not satisfied with these great triumphs, the vascular surgeon today is spreading his way to still greater conquests which have only been possible by the improvement that has been effected by the open surgery of the thorax, a surgery which has been the chief source of all the other triumphs that have been attained in the cure of aortic aneurysms (until the last few years recognized as inaccessible to surgeons and as fatal in their ultimate effects, their existence being usually considered a sentence of death when they were recognized).

Coincident with the great development of the technique most lately devised in dealing with aneurysms of the aorta is the progress made in the preservation of homografts. This real transplantation from the aorta of the cadaver to the site of the attachment of these excised segments and the suturing of the transplants, or grafts, directly to the divided ends of the excised artery have led to the development of a variety of techniques which, in their relation to the various segments of the aorta and its branches, have made it necessary to create a new nomenclature for the methods of this branch of surgery, which is entirely new and strange in anatomic nosology.

I have already referred to the immense progress accomplished in the technical approaches and results of vascular surgery in its relation to the congenital disorders of the heart, including the new surgery of the ductus arteriosus, the stenosis or stricture of the pulmonary artery, coarctations of the aorta with or without their consecutive aneurysms, and the new techniques for their correction and relief. We now come to no doubt the most commanding of all the cardiovascular lesions, which, from as far back as the days of Antyllus and the beginnings of surgery up to the present time, have engaged the attention of surgeons, and at the present, after centuries of experience and labor, have at last come to a hopeful prospect of successful relief and cure with the help of the latest and most advanced improvements in the techniques of attack and cure peculiar to our strictly modern tactics. As previously stated, by the conjoined improvements in the methods of thoracotomy and intrathoracic techniques, we may claim to have attained the maximum of efficiency and accomplishment in the conquest of aortic aneurysms.

I cannot attempt even to mention the vast mass of achievements accomplished in the cure of aortic aneurysms without continuously overlapping and accumulating the number of successes that are being recorded in almost every one of the great surgical world clinics in the recovery and cure of aneurysms of the aorta, which develop in almost every section and branch of this great artery, whether inflicted in injuries, accidents, and diseases of civilian life, or in the more frequent and fatal accidents of war. It will suffice only to mention some of the latest achievements that confirm our confidence in the supreme conquest of aortic aneurysms. Nothing can justify more fairly, justly, and proudly the triumphs of cardiovascular surgery as developed in the field of the aortic distribution than the quoting of a few examples of the many hundreds of successes in the radical cure of abdominal and thoracic aneurysms, as the reports of these heroic episodes in the history of surgery appear in our periodical press almost month by month or week by week.

While the uniform successes and cures resulting from our present methods of dealing with aortic aneurysms fill us with amazement and strengthen our courage and boldness in attacking this hitherto defiant and fatal surgical affliction, we feel that modern scientific surgery has never accomplished its mission with greater glory than it has at this very historic period of our surgical greatness.

Merely because I cannot resist the desire to name and applaud the glorious achievements that the masters of our guild are adding to the luster and worthiness of our profession in dealing with aortic aneurysms, I will mention only a few of the names that occur to me at this moment, without any thought of creating envious distinctions among the great mass of our colleagues, who are now working with marvelous activity for the glory and renown of our art in almost every surgical center of the world. I would only mention such of our fellow members and contemporaries as the following: Bahnson, Blakemore, Brock, De Bakey and Cooley, de Takats, Charles and Claude Dubost, Fontaine, Freeman, Hierton, Hufnagel, Lam and Aram, Monod, Murray, Schafer and Hardin, Shumacker, Swan, and others. De Bakey and Cooley and Schafer and Hardin have reported most notable and difficult operations involving extirpation of aneurysms of the abdominal aorta including the bifurcation of the common iliacs, with restoration of the continuity of the circulation by replacement of the excised segments with preserved or freeze-dried homologous grafts.*

The practicability of shunts has been established for cases in which it is necessary to maintain the circulation and at the same time control hemostasis while extirpating aneurysmal areas of the aortic trunk itself and substituting transplanted grafts. Several reports of the use of shunts to by-pass the area of aortectomies have been published, to the great credit of such operators.

Notable among those who have left distinguished records of the use of shunts in the treatment of aortic aneurysms are such as Carrel and Guthrie,

*In a letter dated July 6, 1953, Dr. De Bakey said, "We have now performed this procedure of excision of aneurysms of the aorta with restoration of continuity by homografts in 21 cases. The results have been so gratifying that we believe it provides the most satisfactory surgical approach to this problem."

whose performances were solely in the animal laboratory, and, clinically, Blalock, Gross, Hufnagel, Shumaker, Schafer and Hardin, De Bakey and Cooley, Bahnson, and others, who worked with various procedures and material.

This dedication also brings to memory Elliott C. Cutler's report as an invited guest before the American Surgical Association in Boston, in April, 1924, of four operations he had performed for the relief of mitral stenosis. It is now thirty years since his first successful attempt was made to relieve a stenotic lesion of the mitral valve (May 30, 1923). This great achievement (first relief of mitral stenosis) is now indelibly associated with the name of Elliott Cutler, for many years surgeon-in-chief of Peter Bent Brigham Hospital in Boston. In this way he realized the dictum and prophecy of Lauder Brunton (1902) of twenty-one years earlier, and which before then was thought of by others.

The first operation performed by Cutler was on a young girl 12 years of age on whom he operated by opening the base of the heart and dividing the obstruction in the valve with a small cutting blade. The patient recovered, was in good condition at the time of his report, and is said to have lived four and one-half years.

While the mortality of the group (one success as a definite cure, of four operations) was apparently discouraging, the success obtained in the first case gave encouragement for future efforts in similar cases. Work being done in St. Louis coincidently with Cutler's work was helpful in encouraging very decidedly the study of the techniques of the operation on the heart, which in the past had so largely deterred experimentation because of the fears of fatality from surgical trauma and manipulations. There was a decided improvement in cardiac work with the realization of the safety of access to the valves by the route of the auricular appendages and also the ability to illuminate the chambers of the heart by an electric speculum while the living heart was functioning, as suggested and applied by Allen and Graham of St. Louis, but never generalized as a practical instrument.

The experimental work being done at the time was also of immense value in demonstrating the enormous importance of animal experimentation in giving encouragement to clinical surgery of the living functioning heart. The great benefits which surgery received from animal experimentation in this field of surgery were stressed in the discussion of Dr. Cutler's paper by Harvey Cushing, W. W. Keen, Crile, myself, and others. Dr. Keen said: "I thank God I have lived to see this domain in which surgery had not entered, entered now definitely and positively!" I myself said: "It is only right and proper that those of us who have lived through the pioneer period of cardiac surgery should appreciate the evolutionary significance of the clinical and experimental accomplishments of Drs. Cutler, Allen and Graham."

The work done in Dr. Cutler's time developed much later into an enormously expanded field of experimental cardiologic surgery and led to an enormous development in the frequency and success of clinical cardiologic surgery.

Following the initiative of Souttar (1925) in entering the heart through the auricular appendage, a great stream of operations have been reported in the last ten years by innumerable operators all over the world, many series numbering in the hundreds and thousands, and, as far as the mitral valvulotomies are concerned, performed in some clinics no less than possibly two to three a week. To this extraordinary activity in this special vascular field is added the still more notable fact that the numerous and increasing technical accomplishments are being exercised with a relatively small mortality which would have been incredible or miraculous even twenty-five years ago.

Correction of special diseases or affections of the valves and their septal defects are commanding the greatest attention at this moment since they present often the most difficult and even impossible techniques for their correction, including mitral, pulmonic, and aortic valvular operations and their corresponding commissurotomies. As the number of operations for mitral stenosis continues to multiply with such low operative mortality as is recorded in the interesting papers of Baker and Brock, Gerbode and Holman, Bailey, Hurwitt, De Bakey, and others, it would seem that the prophecy uttered by Bailey, of Philadelphia, in New Orleans in March, 1949, that the mortality of valvulotomies for mitral stenosis could be reduced to 5 per cent has already been more than realized. Among others distinguished for cardiac surgery are: Beck, Blalock, Glover, Harken, Hufnagel, Levine, O'Neill, Smithy, and others. Without wishing to disturb the modesty of some of my junior friends and colleagues who are shedding luster in our section of the country by their ever-increasing achievements in this special field of surgery, I am still compelled to mention some of my eminent colleagues including Ochsner, Veal (formerly of New Orleans), Burdette, Miangolarra, DeCamp, and Kahle, of New Orleans.

When we consider the enormous development of the surgery of the heart we cannot fail to realize the debt of humanity to the indomitable courage, enterprise, and splendid example set by that intrepid surgeon, Elliott Cutler, who left the seal of immortality on his noble career, to the honor of our guild and of our specialty.

The truth is after all that this phenomenal progress which has been accomplished in the surgery of the blood vessels (arteries as well as veins) has been unquestionably due to several factors which have traveled together on this new road in the last few years. These factors are improved medical techniques favored by the development of a perfected, safer anesthesia, better surgical training, greater knowledge of a previously much-neglected embryology, technical improvements in the instrumentarium, and, last but not least, catheterization and visualization of the interior of the heart via the normal venous and arterial channels (Courand and others). This has been in accord with the increasing number of inventions devised by numerous operators and with the increasing number of discoveries in the field of congenital deformities. In addition, vastly advantageous and almost vital assistance has been obtained from the aid of modern hemotherapy and the relative abundance of the banks of blood, generously provided by the patriotic people of this country. Trans-

fusions and infusions in effective quantities have become most powerful aids to the advancement and safety of surgery of the vessels, as well as of every branch of surgery.

That I have contributed to some extent to the advancement in the techniques and in the safety of vascular surgery in the periphery as well as the visceral domain is a source of profound gratification to me and, I trust, the most valuable of my personal contributions to the progress of surgery.

I feel that it is most gratifying, without the least exaggeration, that one of the simplest things that made the world progress, and probably one of the most attractive because of its very simplicity as well as its antiquity, was learning how to use the needle and thread with all their conservative applications in surgery as a substitute for the far easier, but obliterative, occlusive and crushing ligature. And it is in this simplest and most modest way that time and modern ingenuity have succeeded in elevating the unpretentious needle and thread to the level and rank of the surgical ligature, with its proud history in the vast domain of our surgical art. The comparative history of the needle and of the ligature in relation to their functions in surgery would prove an endless task which, no matter how interesting historically it might be, I will have to omit on this occasion.

My dear colleagues and friends, I am most grateful for the privilege of addressing you on this occasion. It has been a pleasure to recall the history of the Society and some of the more notable incidents that have contributed to the usefulness and happiness of my professional life. And it is an added privilege and grateful satisfaction to have my remarks transmitted directly to you in my compulsory and regretful absence by my very distinguished and honored colleague and friend, Dr. De Bakey.

I am compelled to have this paper read in absentia, which is a source of great regret, since I am not able to renew personally the friendship of numerous colleagues who were with me at the founding of the Society. I am also denied the pleasure of meeting the host of new and relatively young workers who have already left their imprint on the literature of our specialty, who, as future bearers of the torch of progress, are destined to carry the flaming message of the present to the coming generation.

ANTICOAGULANT THERAPY

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THE development of vascular surgery even since the founding of this Society has been truly spectacular. Techniques of entering and leaving the heart and large blood vessels with repair of congenital or acquired damage, restoration of continuity of obstructed arteries, shunts between high pressure and low pressure areas in the portacaval system, repair of aneurysms or their resection, surgery of the sympathetic nervous system for hypertension and peripheral vascular disease, together with blood flow studies in the peripheral or visceral vessels and problems of thromboembolism, have been the topics of our deliberations. Our members have been the leading contributors to these subjects and, through the courtesy of the editors of the JOURNAL, all these papers have appeared in annual numbers since 1948.[1]

In choosing the topic of antioagulants for this address, I have selected a subject to which surgeons were the pioneer contributors. Crafoord,[2] working with the skilled chemistry of Jorpes, and Gordon Murray, aided by Best and his colleagues,[3] were the first to use heparin in surgical patients. This fact needs emphasis, since today the internist, the gynecologist, the physicist, the biochemist, the "coagulationist," and the hematologist are all hard at work at this problem, attacking it from such different angles that conferences on blood clotting seemed desirable for the Macy Foundation in order to integrate accumulating data from such varied sources.[4]

These recent studies have so deepened the seemingly simple theory of blood coagulation that one may well wonder at the temerity of surgeons who grapple with the maze of daily discovered factors of blood clotting. It is my conviction, however, that there is a real need for the establishment of clear-cut criteria for the proper use of the proper anticoagulant and that, as a result of clinical observation at the bedside, some conclusions may even be drawn as to the fluctuations in the state of the clotting mechanism. There is a clinical necessity for a dynamic concept of the hemostatic factors which are not a conglomeration of many ill-defined precursors and proenzymes synergizing and antagonizing each other in a test tube with a multiplicity of nomenclature.[5] The changes in the clotting mechanism should be regarded as an orderly defense reaction against trauma in the broadest sense of the word. The situation is not unlike the one prevailing in the theory of diabetes as against the practical management of the diabetic patient. Certainly the involved mechanism of faulty carbohydrate metabolism, particularly as elucidated by Cori[6] does not directly apply to the clinical evaluation of the diabetic

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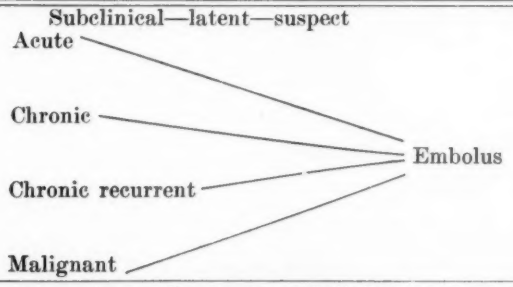
state, which is made by pre- and postprandial blood sugars, the sugar tolerance, and insulin-tolerance curves, methods which are the daily tools of the practitioner of medicine.

I propose, therefore, to discuss this problem along three definite lines, the clinical stages of the thrombotic state, the selection of the anticoagulant, and the conduct of anticoagulant therapy.

STAGES OF THE THROMBOTIC STATE (Table I)

It is certain that a subclinical phase of the thrombocytic state exists which is either symptomless or is accompanied by such vague and nonspecific symptoms that a positive diagnosis is impossible. No one, to my knowledge, has demonstrated any clear-cut changes in the blood in this stage, although later in the discussion I shall present data which would suggest that in certain individuals the natural defense reaction is depleted and that this depletion can be restored, at least temporarily, by heparin. The acute stage, however, whether the thrombus occurs in the calf veins, in the veins of the pelvis, or anywhere else in the body, manifests itself by pain, edema, inflammatory reaction in the lymphatics, fever, leukocytosis, eosinopenia, increased sedimentation rate, and a shortening of the clotting time, especially if this clotting time is sensitized by heparin.[7] The clinical and laboratory findings are produced partly by the effects of local vascular obstruction and a local reaction of the tissues to the thrombus and partly by an alarm-reaction of the body, which will vary from patient to patient. Most importantly, such a patient is heparin-resistant and requires much larger doses of heparin than are customarily prescribed. There is also some evidence of water retention (sodium conservation) at this stage. The process may slowly subside without any specific treatment; in fact, before the days of anticoagulants, when nothing but the prescription of bed rest and bandaging or splinting was done, this was the usual course of events. After six to eight weeks some patients have no further thromboembolic phenomena but are frequently left with persistent postphlebitic sequelae; in a large percentage of cases a chronic recurrent thromboembolic disease results, brought about by the chronic venous stasis in the extremity and partly due to the inability of the clotting mechanism to cope with superimposed aspects of ordinary life such as bed rest, childbirth, operation, trauma, and even emotional stress (Fig. 1).

TABLE I. THE SPONTANEOUS COURSE OF THROMBOEMBOLIC DISEASE*



*Embolus may occur in every stage, also in the subclinical one. Over 50 per cent of pulmonary emboli originate from an unrecognized source.

The thrombotic process may thus heal slowly by lysis or become a chronic recurrent disease, during which thrombi and emboli may occur as late as eight to ten years after the original episode. A study of such a group of patients is

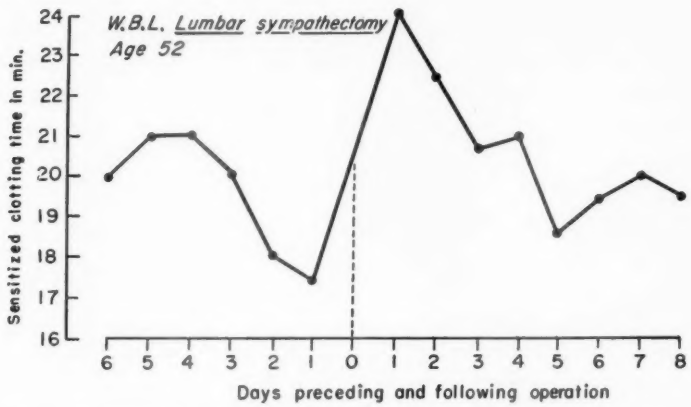


Fig. 1.—Daily clotting times sensitized with 4 γ of heparin per 1 c.c. of blood. In the case of W. B. L. the clotting time gradually shortened before operation and then showed the normal response to surgical trauma after operation. The preoperative drop of the clotting time can be readily observed and can be attributed to preoperative anxiety. Eosinophil counts are also low in the hospital, especially on entrance.

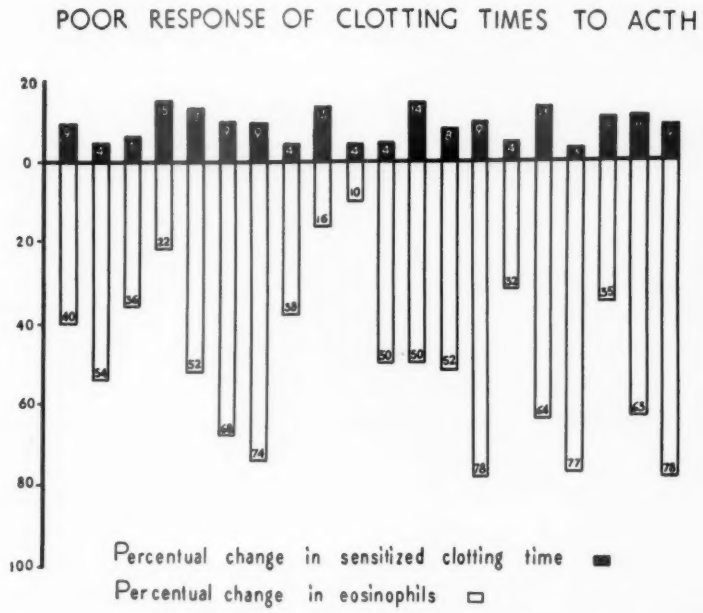


Fig. 2.—Poor response of the clotting mechanism to a single dose of 25 mg. of ACTH in chronic thromboembolic disease.

most revealing, since their clotting mechanism does not respond adequately to a single dose of ACTH (Fig. 2). It is likely that the reported cases of thrombosis following ACTH therapy signify a poor response of the clotting mechanism to a stress, to which it normally responds with hypocoagulability (Fig. 3). If other factors which tend to favor coagulation are present, a real breakdown of the natural defenses against clotting may occur. These occur in patients

who are overoperated, overdigitalized, dehydrated, or desalted, or who have diffuse carcinomatosis or prolonged convalescence (Table II). In such patients, even heroic doses of anticoagulants may not restore the clotting equilibrium to normal. They exhibit one thrombus or embolus after another and usually die of an acute thromboembolic episode. This might be called the malignant phase of thromboembolic disease, representing the stage of exhaustion of the clotting mechanism. I shall point out later that, unfortunately, such a state is frequently iatrogenic, brought about by insufficient dosage or poor timing of the anticoagulant.

TABLE II. FACTORS INFLUENCING HEPARIN TOLERANCE

DECREASED RESPONSE	INCREASED RESPONSE
Advanced age	Youth
Acute thrombosis (first phase)	Acute thrombosis (second phase)
Postoperative state (first phase)	Postoperative state (second phase)
Thrombocytosis	Traumatic } Shock; fibrinolysis
Hemoconcentration	Hemorrhagic }
Polycythemia	Hepatic damage
Digitalis (toxic doses)	Hypoprothrombinemia
Hyperlipemia	Thrombocytopenia
Carcinomatosis	Sodium tetrathionate

Thus, the three stages of thromboembolic disease, the acute stage, the stage of defense, and that of exhaustion, readily fall into the pattern of Selye's general adaptation syndrome,[8] a fruitful hypothesis which we have invoked to explain certain phenomena of both thrombosis[9] and hypertension.[10]

THE RECOGNITION OF THE STAGES OF THROMBOEMBOLIC DISEASE

The acute stage of thromboembolic disease has already been described. It has clinical symptoms and typical laboratory findings. The patient's tolerance to intravenous heparin is increased, the heparin-sensitized clotting time is shortened, and he retains water and sodium. It is interesting that the patient with an acute thrombosis may actually show water retention just as after an operation. The eosinophil count is low (Fig. 4).

This acute thrombotic state may be terminated abruptly by large doses of heparin. Not only is the earliest possible administration necessary, but the size of the dose is also important. Fifty milligrams of heparin given intravenously every three hours in a massive, spreading venous thrombosis is not only useless but may result in a prolongation of the disease[11] toward a chronic recurrent phase with pulmonary emboli. This is such a frequent mistake that a typical case representing our present management will be illustrated.

CASE 1 (No. 13849, St. Luke's Hospital).—M. K., a 63-year-old schoolteacher, was admitted as an emergency on July 9, 1951. While he was shaving in the morning, the left leg became weak and took on a purplish color. There was no pain. A physician was called who referred him first to a neighborhood hospital from which he was transferred in the afternoon to St. Luke's Hospital. Previously he had been treated for bronchiectasis, hypertension, rapid heart, and ankle edema. He had been on digitalis and mercurial diuretics from time to time.

The left lower extremity was greatly enlarged from toes to groin and was bluish purple. The distal one-third of the lower leg and foot was cool; the dorsalis pedis pulse was well made out, but the posterior tibial pulse was doubtful, possibly because of the huge ankle edema. Further investigation in cooperation with Dr. Carl Hedblom revealed generalized hypertensive cardiovascular disease and cardiac decompensation; a cardiogram revealed myocardial pathology; the chest x-ray picture showed an area of infiltration in the left lower lobe of the lung consistent with pulmonary embolism; an uncontrolled diabetes with fasting blood sugar of 360 mg. per cent and nonprotein nitrogen of 40 mg. per cent were also present.

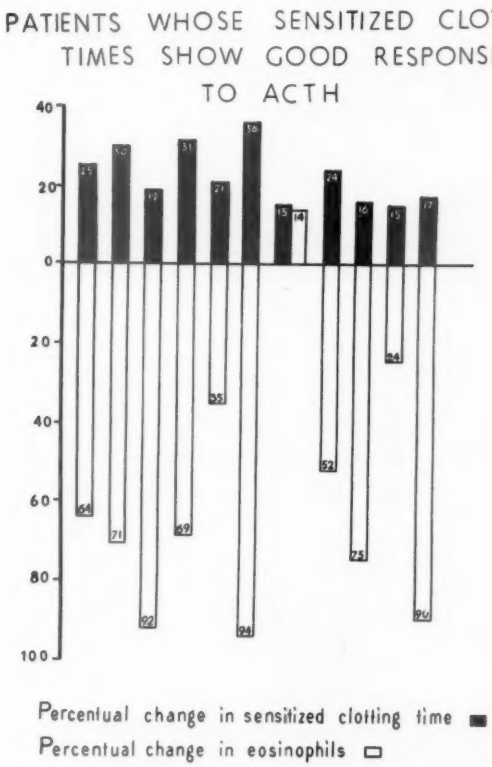


Fig. 3.—The normal response of the clotting time to a single dose of ACTH after four hours. Note the significant rise in clotting times compared to those in Fig. 2, a 15 per cent or larger rise from the preinjection level.

In addition to his medical management, consisting of digitalis, ammonium chloride, regulation of diabetes, and antibiotic therapy, an immediate paravertebral block was performed with little change in the peripheral vascular status. Heparin was started in 100 mg. doses every four hours for two days, which was continued with 1 c.c. of 50 per cent heparin (500 mg.) on the third day. It was soon found that the initially low sensitized clotting time of nine minutes, thirty seconds could hardly be raised with this dosage, so that 1,000 mg. daily doses of heparin divided in two intramuscular doses became necessary. At this stage, 500 mg. of heparin would only produce a rise of the sensitized clotting time to twenty-one minutes, thirty seconds at the third hour with a return to ten minutes at the fourth hour. This dose was reduced on Aug. 18, the ninth day of illness, to one injection of 500 mg. daily and was kept up for another eight days, after which one final injection was given forty-eight hours later. On discharge the patient was compensated without digitalis, the infarct had disappeared on x-ray examination, and the diabetes was under good control.

An interesting change in the thromboembolic disease took place suddenly, by crisis on Aug. 18, 1951. On this day the daily 1,000 mg. dose of heparin had to be suddenly cut in half, the edema and cyanosis suddenly disappeared, and diuresis increased (Fig. 5). This happened without mercurials and was not a digitalis effect since the digitalis had been discontinued four days before. Re-examination seven months later revealed no edema while the patient was wearing long elastic hose. A nylon elastic hose to the knee was ordered.

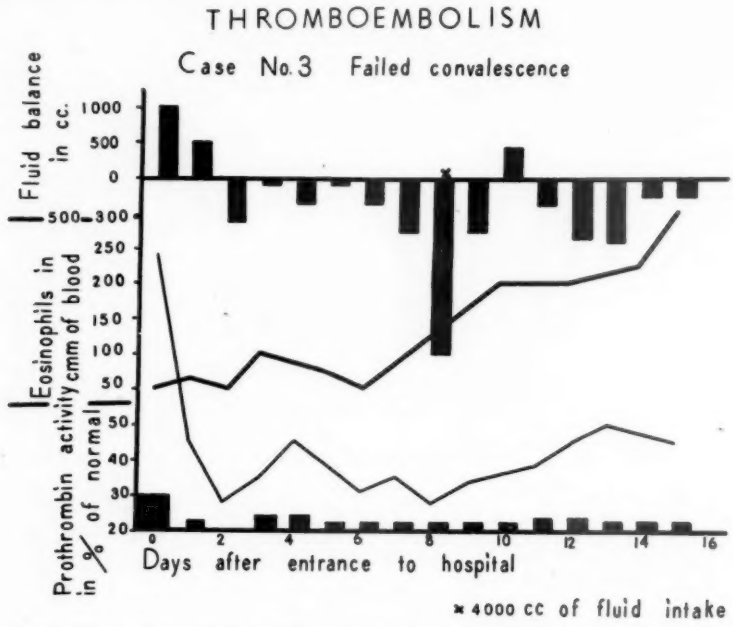


Fig. 4.—Case of E. E. See a detailed analysis of the history under Case 3. Because of insufficient dosage and duration of heparin administration, together with cautious doses of Dicumarol, the disease terminated by slow lysis. Top row illustrates the fluid balance which remains negative. Water retention is greatly accentuated by 4,000 c.c. of liquid intake at asterisk. Eosinophils in the second row climb slowly. Prothrombin activity is depressed below 30 per cent of normal only twice. Patient had a chronic microscopic hematuria because of an old glomerulonephritis.

This man obviously had a lot of complicating factors, in spite of which the transition from a heparin-resistant to a heparin-sensitive state together with marked water excretion is unmistakable. The massive dose of heparin was necessitated not only by the patient's overweight (210 pounds) but also by the extent of the thrombosis, and nothing less than 1,000 mg. of heparin a day was effective. If the massive doses of heparin had been started earlier, the defervescence, diuresis, and loss of edema would have occurred sooner.

Chronic thromboembolic disease frequently results when heparin is stopped too early or too abruptly, or when Dicumarol is used in the acute phase. The duration of treatment must never be less than two weeks nor should the treatment be stopped suddenly. Two cases in point are briefly presented.

CASE 2 (Discharge No. 142022, St. Luke's Hospital).—In 1942, M. M., a 49-year-old executive, developed a thrombophlebitis in the left cubital fossa. This was treated by x-ray and fomentations. It had occurred less than two weeks after the patient donated blood for the Red Cross; in 1949 a similar episode occurred in the right elbow. In De-

cember, 1949, he developed a mild diarrhea, sore throat, and a temperature of 103° F. He remained ambulatory and received two injections of penicillin. Within three days of the onset, right calf muscle pain with cramping on dorsiflexion developed, and he was brought by ambulance to St. Luke's Hospital. On admission the thrombophlebitis seemed to be in the adductor muscle, whereas the tenderness and edema of the lower leg had disappeared. Oral temperature was 101° F. The patient was resistant to 10 mg. of heparin in that the capillary clotting time was two minutes before, and two minutes, ten seconds after, intravenous injection. He received one dose of roentgen ray to the adductor muscle. The following dosage of heparin was used: 100 mg. of heparin intravenously statim, 75 mg. of heparin at 2 A.M. and 7 A.M. the next morning; for the next four days 300 mg. of Depo-Heparin was given daily in two divided doses. On the fifth day, the Depo-Heparin was cut to 200 mg. and on the sixth day it was discontinued. The patient was ambulatory

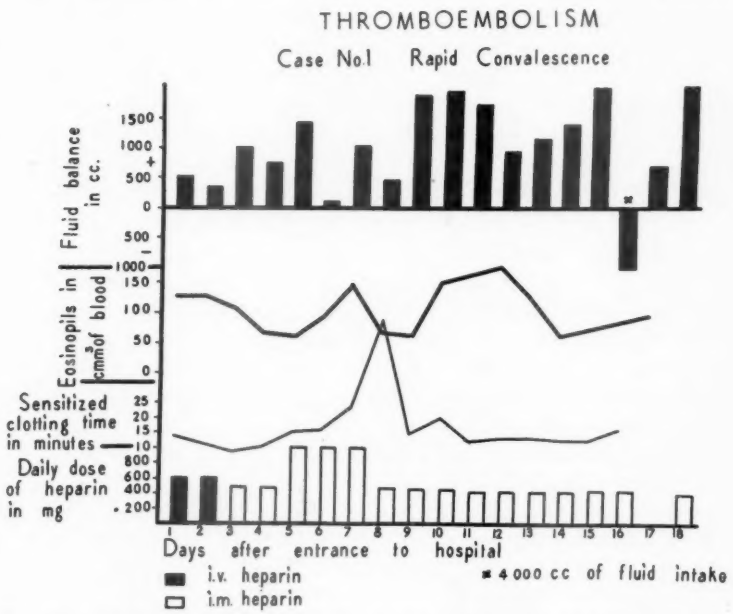


Fig. 5.—Case of M. K. (Case 1 of the text). Compared with Fig. 4, this patient shows a consistently positive fluid balance which only gives way to water retention once (at asterisk), when 4,000 c.c. of liquids was prescribed. Top row illustrates fluid balance, second row eosinophils, third row sensitized clotting times, and fourth row the dosage of intravenous and intramuscular heparin. This patient received 5,200 mg. of heparin during the first week of hospitalization, and the daily 1,000 mg. doses could have been given sooner. The early heparin-resistance is well illustrated, followed after the seventh day by diuresis, rise in clotting time, and increased sensitivity to heparin.

after three days of bed rest and left the hospital on the eighth day. At this time he was free of symptoms and of fever, and the capillary clotting time rose from four minutes, forty-five seconds to seven minutes, fifteen seconds in ten minutes after administration of 10 mg. of heparin. The sensitized clotting time, however (4 γ per cubic centimeter), was twenty-two minutes on discharge, below our normal range for this type of sensitized clotting time. Three days later he was back in the hospital with calf tenderness on the opposite, left side and with a sensitized clotting time of nineteen minutes (4 γ per cubic centimeter). He showed a urinary specific gravity of 1.020 and hematocrit of 49.5 with 12.9 Gm. of hemoglobin. Depo-Heparin was started again in daily 200 mg. doses. He received 200 mg. twice each week for two weeks.

In less than two months the patient entered the hospital again, this time with a deep venous thrombosis of the right, initially affected calf. He received 200 mg. of heparin in the muscle daily, during five days in the hospital, and for a total of two weeks as an ambulatory patient. Efforts to diagnose thromboangiitis obliterans or migrating thrombophlebitis failed. No further attacks were observed for three years after this episode.

The treatment of this patient was faulty in that (1) he did not get enough heparin initially, and (2) the duration of treatment was too short. This and several other experiences led us to the adoption of a two-week period of anticoagulant therapy for acute thromboembolic disease; otherwise, chronic recurrent thromboembolic disease may result.

CASE 3 (No. 31189, St. Luke's Hospital).—Dr. E. E., a 56-year-old surgeon, entered the hospital on July 16, 1952, with a hard, swollen, painful left calf, measuring one inch and one-quarter six inches more below the knee than on the right calf. The pain started three to four days previous to admission. All other findings were negative with the exception of an albuminuria with few casts and red cells, which has persisted since a case of nephritis in childhood. The sensitized clotting time (1 γ per cubic centimeter) was ten minutes, thirty seconds, the normal range varying between twelve and fifteen minutes. Because of the microscopic hematuria, heparin was started intravenously in 50 mg. doses every eight hours on the day of admission and then increased to 100 mg. three times each day for the next two days. The patient was kept ambulatory with an elastic bandage for four days in the hospital and was then discharged with two daily injections of intramuscular heparin, receiving a daily dose of 250 mg. He showed rapid disappearance of the acute phase, the edema and pain disappearing and becoming sensitive to heparin on the fifth day.

He voluntarily stopped the heparin after one week; five days later a right lower lobe embolus occurred for which he was treated by his physician with bed rest and resumption of the previous maintenance dose of heparin, namely, 250 mg. per day. Ten days later, while at home, he experienced a sudden left-sided chest and shoulder pain and was readmitted with the diagnosis of a left lower lobe infarct. The left calf was still turgid and showed pretibial edema. He was in obvious respiratory distress. Roentgen rays confirmed the diagnosis of both pulmonary emboli. The medical department started him on Dicumarol, and prothrombin activity was kept between 40 and 25 per cent of the normal level. Fifty milligrams of heparin was given every four hours for three days. Dicumarol was kept up in doses of 50 to 75 mg. per day, while in the hospital, for seventeen days and has been kept up for three months. Convalescence was uneventful. Fluid balance is shown on the accompanying chart, indicating a long-lasting water retention (convalescence by lysis) (Fig. 4).

The slow recovery of this patient may have been brought about by (1) premature interruption of heparin therapy, (2) insufficient doses of heparin when the first embolus occurred, or (3) the use of Dicumarol which may have dragged out the convalescence and might have led to the necessity of caval ligation had one more embolus occurred.

Actually, we have never seen any bleeding from doses as high as 500 to 1,000 mg. of heparin divided in from four to six daily doses if given in the early acute phase when the requirement of heparin is high. The first phase, especially if adequately treated with heparin, will suddenly give way to the second phase. There is sudden diminution of edema, marked diuresis, a fall in temperature to normal, a rise in the eosinophil count, and a marked sensitivity to heparin (Fig. 5). When this phase appears, the dose of intravenous heparin has to be cut sharply to about 300 mg. of heparin per day in three eight-hour doses. Intramuscular heparin should be given in two doses a day not to exceed 300 to 400 mg. When hemorrhage occurs as a result of too much heparin, it happens in this second phase of resistance, when the natural anticoagulant reaction of the body accentuates the action of heparin.

An identical phase of natural anticoagulant response is observed in the postoperative course of patients. We have previously demonstrated this response of the clotting mechanism to surgical stress[9] (Fig. 6). It can be most simply measured by a single tube venous clotting time sensitized with heparin and calls for immediate reduction of heparin dosage. An analysis of postoperative hemorrhages following heparin therapy[12] shows that they occur in

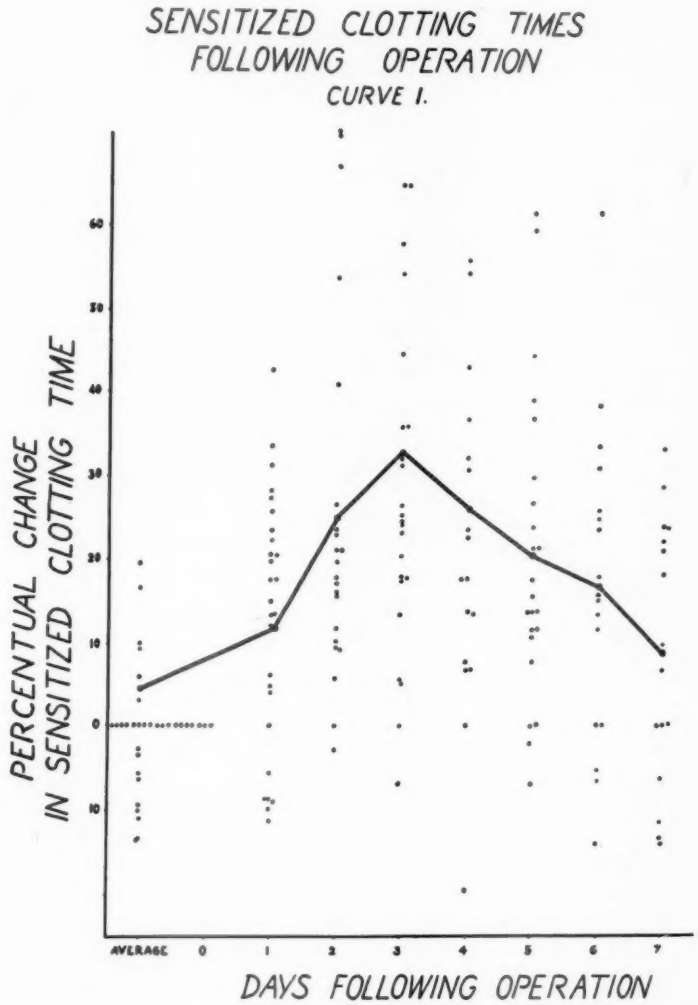


Fig. 6.—The response of the sensitized clotting time to the stress of operation. The peak of the mean curve is on the third postoperative day. (From de Takats and Marshall, SURGERY 31: 13, 1952.)

this second phase of defense, when heparin is added to the natural anticoagulant mechanism of the body. This second phase may last from days to weeks. Two weeks of anticoagulant therapy with heparin is usually sufficient to terminate the acute disease; it is by no means sufficient in an inadequately treated or previously untreated patient who is in the stage of chronic, recurrent thromboembolic disease. Such a patient may not show any laboratory data to suggest an increased clotting tendency; sensitized clotting time, pro-

thrombin level, and prothrombin consumption tests are within normal limits. Such a patient is analogous to the diabetic patient with a normal fasting blood sugar who exhibits an abnormal sugar-tolerance curve after ingestion of carbohydrate. In looking around for a simple, easily reproducible stressor of the clotting mechanism, we have tried several agents. Ten years ago, I described the heparin tolerance which consists of the response of the clotting time to a small dose of heparin[13]; this was later so modified that only two clotting times were determined, one before, and one ten minutes after, administration of 10 mg. of intravenous heparin.[14] Later, we used an in vitro test by placing 1 γ of heparin in the test tube in which a Lee-White coagulation time was determined.[7] More recently, we have applied epinephrine and the ACTH test of Thorn by determining not only eosinophil response but the response of the sensitized clotting time (Figs. 2 and 3), and this I regard a true tolerance test of the clotting mechanism since it places this system under pressure and measures the effect of such a strain on the clotting time. In the chronic recurrent phase of thromboembolic disease, the ACTH test shows a markedly abnormal response. Instead of a normal rise of the clotting time, no response, or a fall, or a rise followed by a fall, a type of withdrawal symptom, may be observed.* Most interestingly, three days of anticoagulant therapy may evoke a better response in a previously poorly responding patient (Fig. 7). The significance of this finding may be utilized in a short preoperative prophylaxis with heparin (Fig. 8).

Every surgeon is familiar with a terminal malignant phase of thromboembolic disease, in which no amount of anticoagulant therapy is of any avail. Such patients are overwhelmed with thromboplastic substances with which they are unable to cope.

CASE 4 (No. 22687, St. Luke's Hospital).—A. H., a 59-year-old, thin, highly nervous woman, entered the hospital in February, 1952. In 1950 she fractured the right hip following which she developed a swelling of the right lower extremity; not long after, a swelling of the abdomen developed. In December, 1951, and January, 1952, bumps developed repeatedly in both lower and both upper extremities. After some delay she entered the hospital, mainly to find, if possible, the cause of multiple areas of phlebitis. Both cubital and both saphenous veins were phlebitic, and a vague mass was palpable in the lower abdomen, mostly to the left. In February, 1952, a large left ovarian cyst was removed by Dr. Eugene Edwards which, on histologic section, proved to be a papillary carcinoma of the ovary. The vena cava was carefully explored but was not ligated because it showed lack of inflammatory reaction around it. Postoperatively, the patient was placed on anticoagulants and received deep x-ray therapy for thirty days, which caused considerable nausea and vomiting.

The clotting mechanism was studied from various angles. Daily sensitized clotting times showed little postoperative fluctuation, but were within normal limits. Twenty-five milligrams of ACTH caused no rise, but produced instead a slight drop, in the sensitized clotting times. Five hundred milligrams of treburon, a heparin substitute, given for three days could not alter this response. Finally, 1,000 mg. of treburon for three days produced a normal response, indicating a marked resistance to anticoagulants (Fig. 7, Case 5). However, on discontinuing the anticoagulant, the response to ACTH was again poor.

*As described in a recent report, Fahey (Proc. Soc. Exper. Biol. & Med. 22: 491, 1951) found no significant alteration of the clotting time after ACTH using a five-tube coagulation time. This does not correspond with our experience (de Takats and Voigt, Angiology 4: 283, 1953).

This patient's unexplained multiple phlebitis led to the discovery of an ovarian malignancy. This was missed by several examiners, including those at a large clinic. The patient exhibited a marked and continuous heparin-resistance for which large doses of a heparinlike substance were necessary. The leg edema remained permanent, but the attacks of phlebitis have not recurred up to this writing (one year).

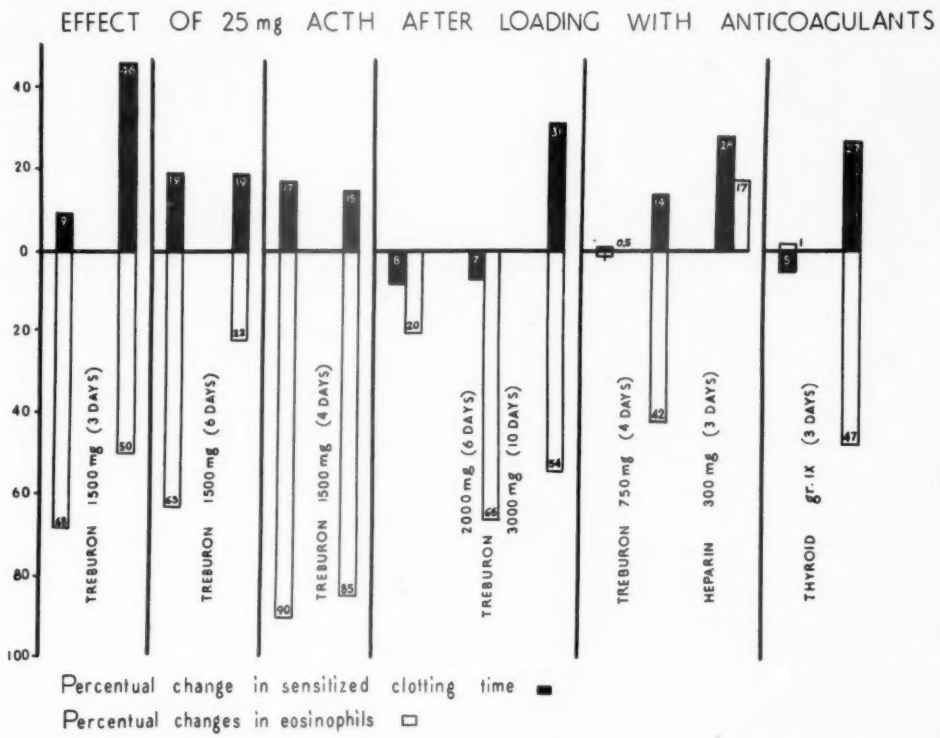


Fig. 7.—The influence of short "loading" anticoagulant doses on the ACTH response. A heparin substitute (treburon) was used for this purpose. In the second and third patients, the ACTH response was unimproved. They did not receive enough anticoagulants. Cases 1, 4, and 5 showed a normal response after an initial poor response. In Case 6, the normal response was restored by thyroid medication (de Takats and Voigt, Angiology 4: 283, 1953).

In the malignant phase, ordinary methods of anticoagulant therapy by intermittent intravenous, intramuscular, or subcutaneous routes are of little avail. Possibly, this is the field for the continuous intravenous drip with heparin, but the customary daily doses of 300 to 500 mg. are surely inadequate.

These, then, are the syndromes which require anticoagulant therapy. We can now discuss the available anticoagulants and their methods of administration.

THE ANTICOAGULANTS

Heparin.—The cost of heparin is still a potent deterrent, but this is gradually decreasing. Drug sensitivity does exist, and I reported such cases in our early experience.[13] Not only do such patients exhibit flushing of the face, dyspnea and bronchospasm, but the clotting time is markedly prolonged. Such

sensitivity reaction may be avoided by using a 10 mg. test dose on every patient who is to be heparinized. This drug sensitivity is not so uncommon as most investigators believe. It occurred in 8 per cent of 256 patients.[14]

Heparin, as we have pointed out elsewhere, is not only an anticoagulant; it has an antiphlogistic and an antihyaluronidase effect[15] and it is often a cause of eosinophilia.[9] It may influence antigen-antibody reactions. When clotting curves are plotted together with eosinophil counts, it will be noted that the latter often rise together with the anticoagulant effect, although possibly independently from it (Fig. 9). As Kark and his associates have shown at our institution,[16] heparin counteracts the eosinopenic effect of cortisone in vitro and thus spares the eosinophils. Its beneficial effect in gout has recently been reported.[17] Heparin also has an effect on serum lipoproteins and has been advocated for the treatment of coronary atherosclerosis.[18]

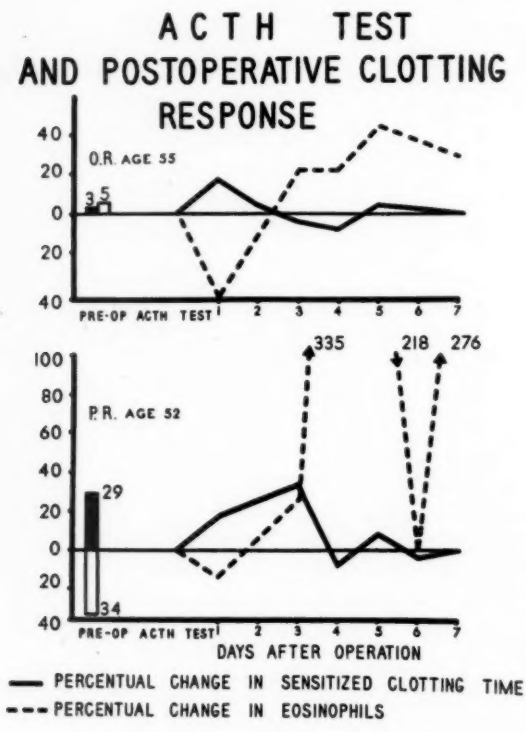


Fig. 8.

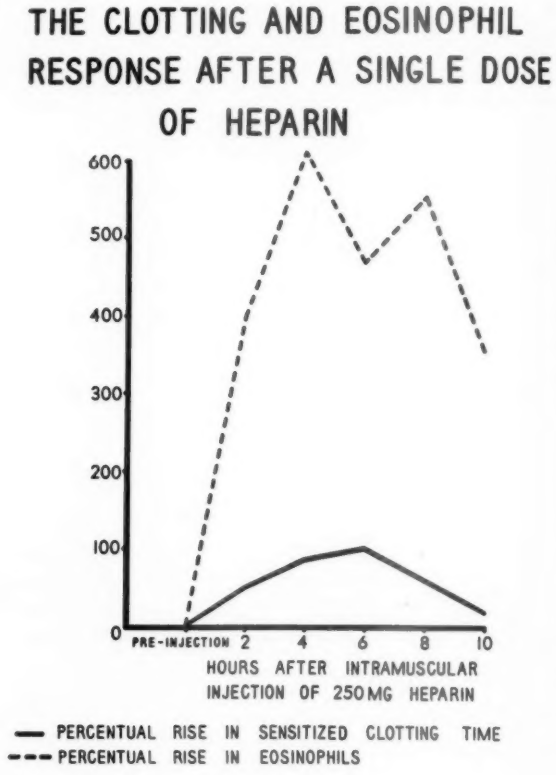


Fig. 9.

Fig. 8.—Postoperative clotting curves of patients who have received heparin preoperatively for three days.

Fig. 9.—Correlation of preoperative ACTH test and postoperative clotting response.

The intermittent intravenous administration of heparin has been an excellent method in our hands, and the commercially available 1 per cent solution can be given slowly, undiluted in 100 to 150 mg. single doses. Fifty per cent heparin in aqueous solution, mixed with 1 c.c. of 1 per cent procaine is an ideal way to give 250 to 500 mg. of heparin subcutaneously in small volume. It is unfortunately not marketed; however, 10 per cent aqueous solutions are

readily available. We prefer it to heparin in retarding medium of gelatin and dextrose, after having extensively studied such a preparation,[19] which is painful, viscous, and not tolerated as well as the aqueous solution. If it were certain that the evenly elevated, plateau-shaped clotting times which follow the administration of Depo-Heparin are preferable to the spiked curves of the aqueous heparin, then heparin in retarded medium would be more advisable (Fig. 10). It is not all clear at the moment, however, that what is needed is the filling up of heparin stores rather than a certain arbitrary level of elevated clotting time.

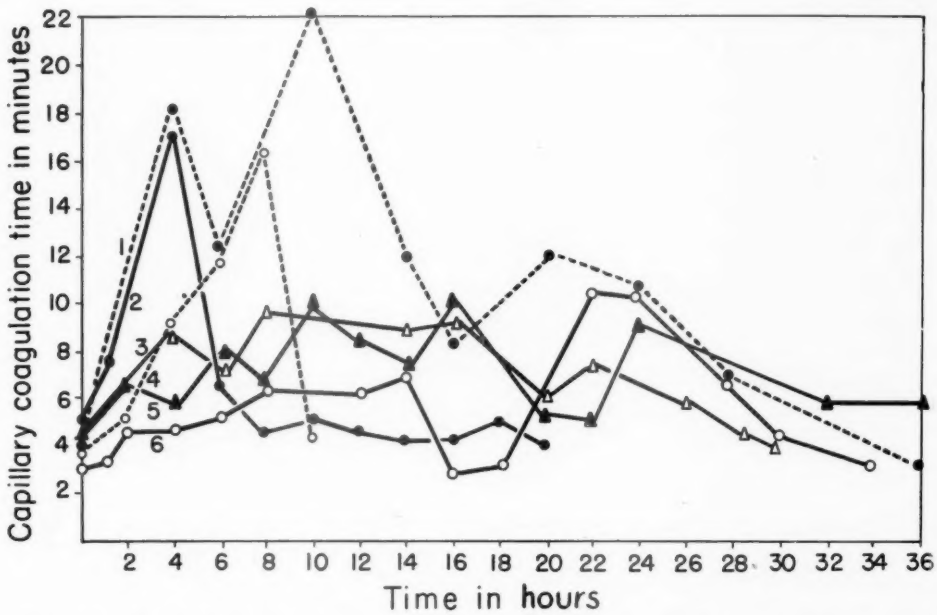


Fig. 10.—Serial determinations of clotting times obtained after Depo-Heparin. Each line represents an average of ten patients studied. The solution containing 400 mg. of heparin with vasoconstrictors (Line 4) showed a plateau-type of response from thirty to thirty-six hours. (From de Takats, J.A.M.A. 142: 527, 1950.)

Heparin substitutes, namely, Paritol, thrombocid, and treburon, have been available for clinical investigation for some time. Of these we have not investigated Paritol,[20] a polysulfuric ester prepared by the sulfation of alginic acid. The side reactions of this drug are so severe that its clinical use has little justification, all the more since the amount of Paritol sufficient to obtain an anticoagulant effect is thirteen times that of heparin. The side reactions consist of nausea, vomiting, abdominal cramps, and occasionally a fall in blood pressure. Link[21] has pointed out that sulfuric acid esters of carbohydrates tend to produce clumping of platelets resulting in platelet thrombi in organs such as liver, lungs, and kidneys. The thrombocytopenia occurs within thirty minutes after intravenous injection, and in the case of chitin disulfuric acid, 1 mg. given intravenously produces a fall of 10,000 thrombocytes per cubic centimeter of blood.[22] Because of this experience, primarily emphasized by Astrup and his associates,[23] we approached two other sulfurated polysulfurides, namely, thrombocid and treburon, rather gingerly. With the

former, studied experimentally with Dr. Last and clinically at the hospital, we obtained good effects in individual tolerance curves in doses which were three times as large as heparin. This meant that in the average hospital patient, weighing about 150 pounds, 450 mg. of thrombocid was needed for prophylactic, and at least 900 mg. of the drug for therapeutic, purposes. There was then too much bulk (3 to 6 c.c. of the 5 per cent solution three times a day) to be injected. Also, the solution was very acid and burned considerably. While these drawbacks could have been readily corrected, most importantly, after repeated doses, decrease in platelet count and alopecia occurred, for which reason our group abandoned its use.[24] The third synthetic preparation, treburon, was given an extensive trial mainly in the form of intramuscular injections; there were no side effects on single intravenous doses. Again, the clotting time raising effect was three times that of heparin. When it was given in daily therapeutic doses to patients suffering from thromboembolic disease, a satisfactory effect was produced. However, in four of five patients receiving more than a total of 2 Gm. of the drug, a massive alopecia occurred two to three months after the drug was discontinued. Platelet counts of these patients, taken during the administration of the drug, were at the lower levels of normal (150 to 200,000 platelets per cubic millimeter of blood).

There is also the temptation to study these interesting drugs in regard to their anticortisone effect. All synthetic heparinlike substances, including heparin, produce eosinophilia, but this effect may have nothing to do with their anticoagulant property. Heparin itself has platelet clumping properties as studied by Copley,[25] and there is one well-documented case of alopecia following heparin, published by Merz.[11] Because of many hundreds of patients who have received heparin in our clinic without exhibiting alopecia, it is reasonable to believe that this is due to some impurity in heparin which is not contained in some preparations.[26] We have concluded, then, that no adequate substitute of heparin has yet been synthetized, but that there is good hope that, if the radical containing the platelet-clumping property can be eliminated, an inexpensive intravenous and intramuscular administration of such a drug may well be feasible.

PROTHROMBIN-DEPRESSANTS

These substances act by inhibiting the formation of prothrombin in the liver. Following the extensive use of Link's ingeniously discovered substance, Dicumarol,[27] a number of later substitutes, namely, tromexan, Cyverine, and phenylindanedione, have been marketed. Of these drugs, phenylindanedione (PID) is a prothrombinopenic agent although not a coumarin. The decrease in prothrombin level occurs as early as twelve hours after oral intake of 10 to 20 mg. per kilogram of body weight, and return to normal is reached in ninety-six hours. It is the V factor of Owren which seems to be depressed by the drug, again an example of an anticoagulant which does not affect the third phase of clotting, that is, the transformation of thrombin to fibrin.

The advantages and disadvantages of these substances have been discussed elsewhere,[14] and I hasten to say that it is not unfamiliarity with these

compounds which makes one so hesitant to use them, but the conviction that they do not affect the total clotting mechanism and that in their present usage throughout the country the balance is more against them than in their favor. In the first place, their oral use and their inexpensiveness make them especially dangerous. They may be and are being taken for prolonged periods, in some instances for as long as two years. The present laboratory control is obtained by single-stage or two-stage prothrombin determinations, and the best thought today is that these determinations really do not measure prothrombin levels but are, at best, accelerated clotting times. As a matter of fact, both the heparin-sensitized clotting time and the clotting time in lusteroid or siliconated tubes show a definite response to the coumarins (Fig. 11) and, although a systematic and rather expensive organized effort has been made to teach prothrombin determinations to laboratory technicians throughout the country,* there is a serious question in the minds of many workers as to what the significance of the single-stage prothrombin time is and how well it controls the action of the coumarins. Aside from the shakiness of the laboratory control, the question arises as to whether depressing the prothrombin level to 20 per cent of normal is actually an adequate safeguard. There is clinical evidence to show that with a 20 per cent prothrombin level, hemorrhage can occur.[28] These laboratory data came from leading clinical laboratories of the country. The argument then is not so much against these prothrombin-depressant drugs as against their present laboratory control. If heparinized or siliconated test tubes were readily and commercially available, the action of these prothrombin-depressant drugs would be more simply controlled.

Perhaps the greatest argument against the coumarin series is that small doses seem to increase the clotting tendency, possibly through increased fibrinogen levels.[29] Thus, in a previously published graph (Fig. 12), one notes that with a slow fall of the prothrombin level an initial shortening of the clotting time occurs. Since many internists are in favor of so-called "cautious" doses, it is indeed possible that the prolonged use of small doses of dicumarol may increase the tendency to blood clotting. This thought has also been expressed in regard to heparin; we ourselves have observed a rebound-phenomenon to exist.[14] Again and again one sees patients who develop a thromboembolic episode after the anticoagulant has been stopped. The interpretation of this finding has been that the drug has been stopped too early. However, it may well be that the balance of the clotting equilibrium which has been shifted over to the anticoagulant side has now been permitted to swing to the coagulant side. Very little factual knowledge exists about these phenomena, but a kinetic concept as expressed by Garrott Allen[30] in his "hemostatic homeostasis" should deserve much consideration.

PURIFIED TRYPSIN

As a result of a report of Innerfield and his associates[31]† experimental material was obtained for clinical trial and given in doses of 100,000 to 150,000

*American Heart Association cooperating with the Public Health Service.
†Courtesy of Dr. Marvin Zyporin, The Armour Laboratories, Chicago, Ill.

U. dissolved in 500 c.c. of physiologic saline solution once or twice a day by slow intravenous drip. Because of the frequency of chills, pain, and thrombosis at the site of the injection, only a few clinical observations were made. There was no detectable change in the sensitized clotting times. The serum globulin seemed to drop, but not the serum albumin. Sodium diuresis occurs after

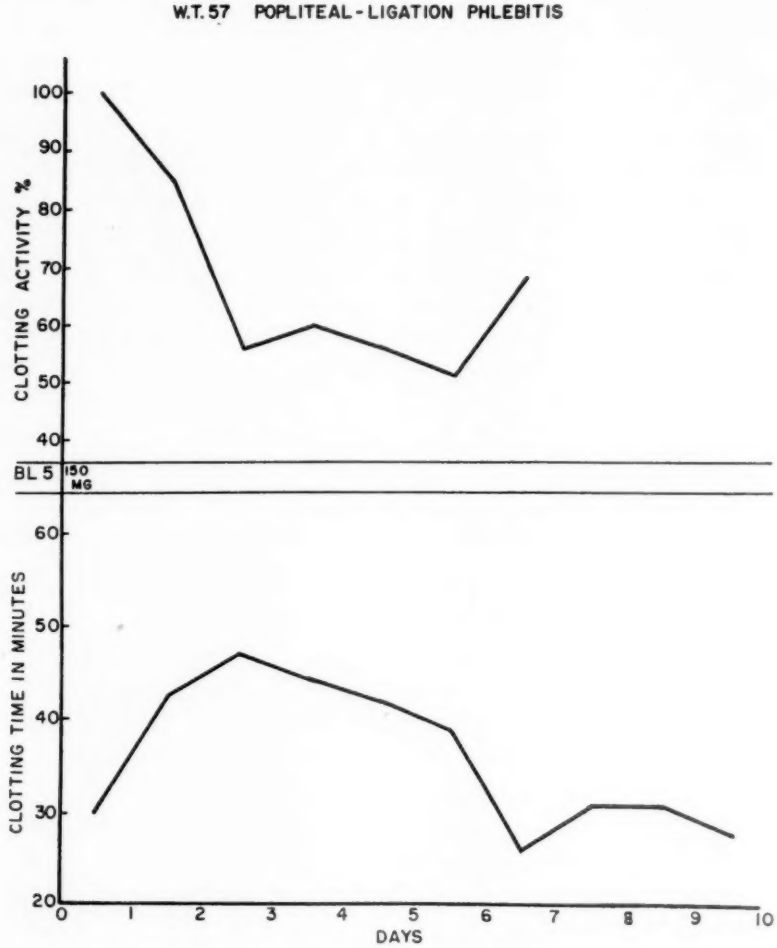


Fig. 11.—Effect of a single dose of coumarin on prothrombin activity and sensitized clotting time (4 γ per cubic centimeter). Note the almost mirror image of the two curves. The clotting curve reaches its peak one day sooner and its downward slope is more gradual. (From de Takats, Angiology 1: 317, 1950.)

initial conservation. The clinical response seemed no different from that obtained many years ago by the injection of triple typhoid vaccine in small subreactionary doses.[32] The degradation products of proteins, particularly those of fibrin, may well give rise to a series of hormonal or enzymatic reactions, but at present there is no justification for continued clinical use of this product which meanwhile deprives the patient from receiving heparin.

THE CONTROL OF HEMORRHAGE DURING ANTICOAGULANT THERAPY

Heparin and Substitutes.—Hemorrhage as a result of heparin administration is of two types. The one is due to overdose and can be readily controlled

by protamine or toluidine blue. The protamine effect lasts about four hours, a 1.5 to 1 ratio being entirely suppressive of heparin action, 10 mg. (10 c.c.) being the usual dose; toluidine blue has a much longer action and stops bleeding in any state in which an increase of heparinoid substances is demonstrable by protamine titration. Toluidine blue is given in doses of 2 mg. per kilogram of body weight intravenously over a period of two hours in 500 c.c. of physiologic saline solution. While this dye is hemolytic in normal dogs, no such reactions have been encountered in man. Uncontrolled hemorrhage from heparin, or

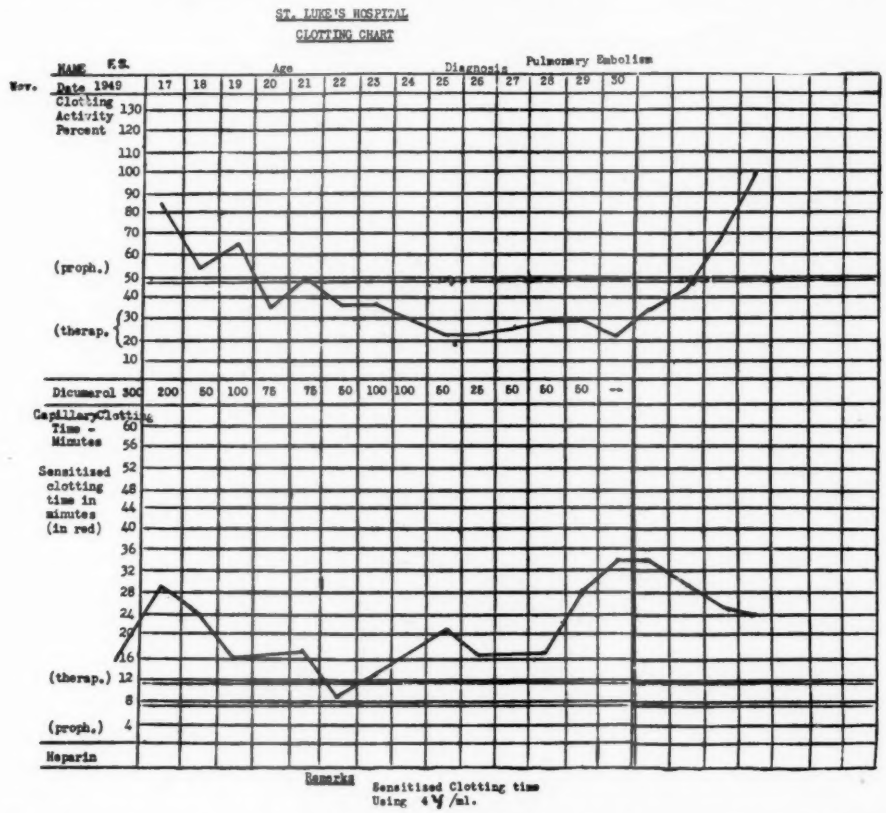


Fig. 12.—Simultaneous prothrombin levels and sensitized clotting time curves in a patient who developed pulmonary embolism at bed rest. Note that the prothrombin levels drop very slowly because of "cautious" dosage and that the clotting times shorten at first. Actually the therapeutic levels were not reached according to clotting times until the thirteenth day, and according to prothrombin levels on the ninth day. The pattern of this graph may be interpreted as resulting from the stimulating effect of small doses of Dicumarol on fibrinogen production in the liver. (From de Takats, Angiology **1**: 317, 1950.)

hemorrhage controlled after too much delay, produces a second hemorrhagic state which is not now neutralized by protamine sulfate or toluidine blue. This situation may also occur after overdosage with Dicumarol, and it is due to the excessive hemorrhage per se producing a shocklike state in which fibrinolysin appears.[33] Blood transfusions, which are of course our best standby in any type of hemorrhage, may increase hemorrhage if not very carefully cross-matched.[34]

Coumarin and Other Prothrombin Depressants.—Hemorrhage from Dicumarol is treated by oral and intravenous doses of vitamin K_1. One hundred

milligrams intravenously brings the prothrombin level back to a safe range in about four hours. A recent intravenous preparation of emulsified K_1 is highly efficient. In addition, blood stored for not more than a few days is a potent source of prothrombin for the prothrombin-depleted patient. In the case of phenylindanedione, the oily suspension of K_1 is active. The sudden return of the prothrombin-range to safe levels either by vitamin K_1 preparations or by blood transfusion may bring on another thromboembolic episode. Such a case was published by Fowler and myself early in our experience with Dicumarol.[35]

DISCUSSION

This brief survey is not intended to be a summary of the literature on anticoagulants. It is simply based on personal observation of a small number of patients serially studied. This method of approach has been decried by those who do not believe in any valid conclusions unless they are based on about 1,000 statistically analyzed cases. Such data, however, may be so handicapped by faulty observations and nonrecognition of significant variables that even the most skilled statistician may come to the wrong conclusions. After all, the basis of his mathematic formulae is still the observation of the individual patient and not the "average behavior of the case." For this reason the present type of study is focused on the recognition of different phases of thromboembolic disease by simple clinical means and the administration of heparin, our best anticoagulant to date, in sufficient doses with proper timing. I have not discussed the place of proximal vein-ligation in the treatment of thromboembolic disease because our attitude has not changed since our initial publication on the subject.[35] Superficial femoral vein ligation or ligation of the vena cava is practiced (1) when the patient cannot be given any heparin, and (2) when, in spite of adequate heparin dosage, thromboembolic phenomena continue. It might be well, however, to qualify these two indications. Patients cannot be given heparin if they have a large mucosal defect in the gastrointestinal or genitourinary tract, and in such cases it is better to give no heparin than to give a little heparin. A little heparin, as pointed out by Jorpes[11] and by Merz,[11] may do more harm than good. Also, patients with hemorrhagic diseases, notably thrombocytopenia, do not tolerate heparin without intractable hemorrhage.

Regarding the recalcitrant case of the patient who continues to throw emboli during anticoagulant therapy, many times this situation is iatrogenic. The patient did not receive enough heparin, or he was started on Dicumarol which was cut so as to keep the prothrombin level at a "safe" range. It should be remembered that it is far easier to perform a vena cava ligation than to straighten out a patient's badly deranged clotting mechanism. Nevertheless, as a lifesaving measure, to prevent fatal pulmonary embolism, vena cava ligation has a definite place. During the last ten years it has been performed twelve times while treating 235 patients with severe recurrent thromboembolic disease extending above Poupart's ligament.

SUMMARY

Three phases of thromboembolic disease are recognized. In the first, acute phase, characterized by local symptoms and a general reaction of the body to a stressor stimulus, large doses of heparin are recommended. For the second phase, the body's own defense mechanism is beginning to work, and heparin-dosage has to be sharply cut or otherwise hemorrhage may occur. If properly treated, this phase then leads to a third phase of recovery in about two weeks. If not treated or insufficiently treated, a phase of delayed convalescence or "failed" convalescence appears, leading to chronic recurrent thromboembolic disease. If this is not arrested or if overwhelming thromboplastic substances are being continuously formed as occur in some cases of carcinomatosis, a terminal malignant phase supervenes which corresponds to a total exhaustion of the clotting mechanism. Heparin is still regarded as the best anticoagulant; its adequate use by surgeons should be studied as carefully as a technique of vena cava ligation or thrombectomy.

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SURGICAL CONSIDERATIONS OF EXCISIONAL THERAPY FOR AORTIC ANEURYSMS

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ANEURYSM of the aorta has long been recognized as a grave disease producing in most instances disabling symptoms and ultimately death by rupture and hemorrhage. The fact that in patients with aneurysm of the thoracic aorta the expected survival period is relatively short is not fully appreciated. From an analysis of a series of 1,113 patients with saccular aneurysm of the thoracic aorta, Kampmeier[26] concluded that the average expected duration of life after the onset of symptoms was six to eight months, varying somewhat with the level of involvement. Admittedly, an occasional striking exception will occur as exemplified by Kampmeier's report of two patients surviving fourteen and fifteen years, respectively. In contrast to the syphilitic origin of most aneurysms of the thoracic aorta, those involving the abdominal aorta are most commonly arteriosclerotic in origin and affect males usually of advanced years. Estes[20] estimated that only 10 per cent of patients with abdominal aneurysm aged 65 years will survive eight years, whereas 65 per cent of normal persons of this age have a life expectancy of this duration. He also observed that 33 per cent of the patients with arteriosclerotic aneurysm of the aorta will die within one year, in the majority of instances from rupture. Thus, it appears that although the prognosis of arteriosclerotic aneurysm of the abdominal aorta is somewhat less serious than that of arteriosclerotic aneurysm of the thoracic aorta, the prognosis in all aneurysms of the aorta is sufficiently poor to demand prompt and definitive treatment.

The development of an effective method for the surgical management of aortic aneurysms has been actively pursued for nearly one century. In general these efforts have been directed toward obliteration of the aneurysm by attempting to promote thrombosis within the sac by ligation, introduction of foreign material, or stimulation of periarterial fibrosis, but without notable success.

Ligation of the parent artery is one of the oldest forms of treatment, and has been used primarily for aneurysms involving the peripheral arteries. Application of the ligature proximal to the aneurysm as described by Anel,[3] in 1710, has not been satisfactory for lesions of the aorta. Failure has resulted from ischemic changes distal to the ligature and from secondary hemorrhage produced by gradual erosion by the ligature. Attempts to overcome these

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difficulties by use of metal or aluminum bands were unsuccessful.[24, 30] Gradual occlusion by repeated operations, special clamps, elastic band compression, or fibrogenic agents have likewise not been satisfactory. Staged procedures designed to allow time for development of collateral circulation to the distal parts have been unsuccessful with few exceptions. The discouraging results of partial or complete ligation of the aorta for aneurysm have recently been compiled by Croot,[14] who found that all of the twenty-one cases recorded prior to 1918 terminated fatally and that the aneurysm could be considered cured in only four of twenty cases reported since that time.

Application of the ligature distal to the aneurysm as described by Brasdor,[10] in 1798, or both proximal and distal to the lesion, known as Pasquin's operation,[35] has also not proved satisfactory. Whereas in vessels smaller than the aorta complete occlusion may be tolerated if collateral circulation is sufficiently developed, acute occlusion of the aorta, particularly above the abdominal visceral branches, is almost certain to result in failure. For aneurysms of the major tributaries of the aortic arch, Guinard,[23] on the basis of the Brasdor principle, advocated ligating the carotid and subclavian arteries in the neck distal to the lesion. Perhaps combined with other measures such as intrasaccular wiring or fibrogenic agents this technique may have some usefulness. Subsequent revascularization of the lesion is always a threat that is further enhanced if infection supervenes because of the likelihood of secondary hemorrhage. In addition to the attempts to ligate the parent vessel itself, the proximal ligation principle has also been applied to the neck of sacciform aneurysms of the aorta with equally poor results, because of the consequent ischemic changes that occur in the distal portion of the sac.

Introduction of various foreign materials constitutes another method which has long been advocated to promote thrombosis and obliteration of the aneurysm. Among the different materials used, various metals in the form of wire or springs have been most commonly employed for this purpose. The most popular application of this method has consisted of the insertion of various lengths of wire into the aneurysm as originally advocated by Moore,[32] in 1864. Corradi,[13] in 1879, added to this method the passage through the wire of a galvanic current. Since then this method has been revived and modified from time to time in an effort to achieve satisfactory results. In recent years Blakemore,[8, 9] who modified the procedure to provide a more accurate means of applying the electrothermic principle, and Linton[28] have reported encouraging results with this method, but its curative value remains limited.

Fibrogenic materials applied around the aneurysm and parent vessel have also been advocated and used to provide reinforcement and gradual constriction. Based on Page's[34] original observation of the irritating properties of cellophane wrapped around the kidneys of dogs to produce experimental hypertension and its experimental use by Pearse[36] to produce gradual occlusion of large arteries, Harrison and Chandy[25] employed the method in the treatment of an aneurysm of the subclavian artery. With Yeager and Cowley's[43] subsequent identification of dicetylphosphate as the fibrogenic agent, it became possible to select cellophane-polythene films having more con-

sistent fibroplastic response. This method has gained considerable popularity in recent years, and a number of observers have reported encouraging results following its use, particularly in the form of palliation. There is little evidence, however, to support the belief that this method has actual curative value. Thus, Abbott,[1] in his analysis of thirty-two patients with thoracic aneurysms treated in this manner, observed that life was not prolonged in any of the patients with advanced disease, the only beneficial result being relief of pain in about 40 per cent of the cases.

For a number of reasons we believe that this method has limited value and under certain circumstances may be harmful. For one thing, it is usually not possible to surround the aneurysm completely and thus provide reinforcement of all parts of the aneurysm, especially the weakest points usually adherent to adjacent structure. This is especially true of aneurysms that are expanding and eroding bone and other structures. For another, the gradual and delayed production of fibrosis by this method may not occur sufficiently soon to prevent rupture of the aneurysm. Still another, and perhaps the most important, unfavorable effect of this method is its tendency to devitalize the sac. In mobilizing the aneurysm to apply the cellophane-polythene film, the major blood supply to the sac arising from the surrounding structures is interrupted. The application of the film then serves as a permanent barrier to the process of revascularization. The sac wall then lies between a degenerating and liquefying laminated thrombus and the inert film. Thus, although fibroplasia may take place outside the film, the tendency for the devascularized wall of the aneurysm to rupture is enhanced.

That these are not entirely theoretical considerations is evident from recent observations on five cases of aneurysms of the abdominal aorta previously treated by cellophane wrapping and subsequently resected.[18] The interval between the cellophane wrapping procedure and subsequent resection of the aneurysm was forty-one months, twenty-three months, thirteen months, nine months, and eight months, respectively, in these five cases. This is certainly adequate time for the production of an appreciable degree of fibrosis. Yet the perianeurysmal fibroplastic reaction was both grossly and histologically insufficient to provide significant reinforcement. This is shown by the fact that the patients' symptoms continued and the aneurysms progressively enlarged. It was also evident from the histologic studies of the aneurysmal wall that the degree of surrounding fibroplasia is insignificant. It is possible that some of the disadvantages of the cellophane-polythene film may be avoided by the application of the fibrogenic agent, dicetylphosphate, in the form of an injectable suspension as advocated by Berman and his associates.[5]

Endoaneurysmorrhaphy was originally described by Matas,[29] in 1888, and subsequently developed as an obliterative, restorative, and reconstructive procedure.[30] Based on the principle of intrasaccular suture it provided a number of advantages over previous methods by achieving obliteration of the sac without injury to adjacent structures, particularly collateral vessels. This method constituted one of the most important landmarks in the surgical treatment of aneurysm, and for over one-half century it has enjoyed wide use-

fulness, particularly in the treatment of aneurysms involving peripheral vessels. In aneurysms of the aorta, however, the procedure has limited application. This is illustrated by the fact that the method has only rarely been employed in such aneurysms.[6]

Excision of the aneurysm appears to offer the most effective method of surgical treatment. The fact that extirpation has been attempted so infrequently in the past is perhaps due to a number of technical difficulties making the procedure hazardous. In this regard the experience of Tuffier,[40] in 1902, is particularly noteworthy. At operation in a patient with a saccular aneurysm of the ascending aorta, Tuffier succeeded in encircling the relatively narrow neck of the lesion with two catgut ligatures, thus occluding the inflow and partially emptying the sac. He apparently considered excising the sac at the time, but because he thought the presence of the sac would prevent slippage of the ligature and possibly limit hemorrhage if this occurred, he decided not to remove the sac. Gangrene of the sac led to infection and secondary hemorrhage, and the patient died thirteen days later. Tuffier's next attempt was made in 1909 but, unfortunately, during the dissection the aneurysm was inadvertently entered, and although the patient survived the operation, he died two days later.[41] Since that time few cases of extirpation of aneurysms of the aorta or its major branches have been recorded.

Recently we collected from the literature all of the cases of aneurysms of the thoracic aorta and its major branches treated by excision.[12] These could be conveniently divided into two groups depending on whether or not there was an associated coarctation of the aorta. In cases with coarctation, the aneurysm typically appears distal to the constriction and is probably related in some manner to the factors producing poststenotic dilatation in such vascular anomalies. Excision of aneurysms of this type involves less surgical risk to the patient because of the reduced intraluminal pressure and the presence of well-developed collateral vessels supplying the lower half of the body if occlusion of the aorta is necessary. Alexander and Byron,[2] in 1944, reported the successful removal of such a lesion but did not attempt restoration of aortic continuity as was done by Shumacker.[38] Using an aortic homograft, Swan[39] bridged the defect remaining after a similar excision, and more recently, Gross[21] reported five such cases. We were able to find only three successful cases of excision of aneurysms involving a portion of the thoracic aorta and not associated with coarctation. Ochsner[33] described a case in September, 1945, in which a suspected neurogenic tumor of the mediastinum proved at thoracotomy to be a saccular aneurysm of the aorta. The neck of the aneurysm was clamped, the sac excised, and the resultant aortic defect was sutured. The patient subsequently recovered uneventfully. A somewhat similar case was reported several years later by Monod,[31] who excised an aneurysm of the aorta distal to the left subclavian artery and then sutured the defect. Another case of this type has also recently been reported by Woods and Kenney,[42] who, instead of excising the aneurysms and because it was considered the safer procedure, obliterated the aneurysm by infolding and tamponading the sac against the approximated edges of the defect. Blakemore[7] referred

to another case of an aneurysm of the innominate artery which involved the origin of that vessel, and although the precise nature of the findings and procedure were not clear, it appears that he excised the lesion and sutured the aortic defect.

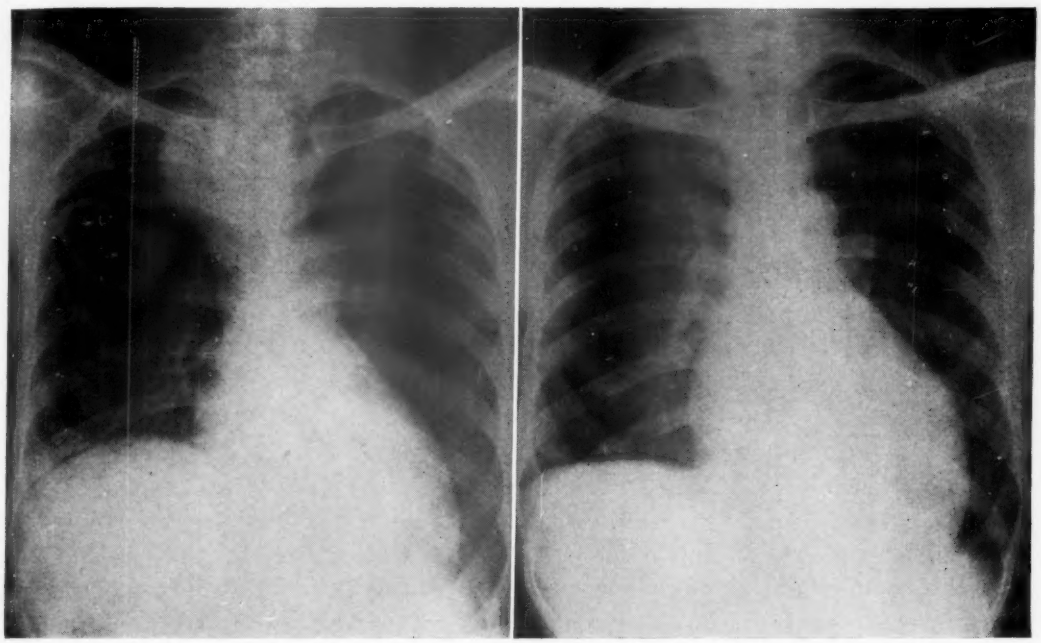


Fig. 1. Fig. 2.

Fig. 1.—Roentgenogram of chest showing upper right mediastinal shadow representing aneurysm of innominate artery and adjacent aorta.

Fig. 2.—Roentgenogram of chest of same patient as in Fig. 1 taken twenty-three months after excision of aneurysm and aortorrhaphy showing return to normal appearance.

We reported on two patients in whom aneurysms of the thoracic aorta were removed by tangential occlusion of the neck of the sac and lateral aortorrhaphy, and advocated excision of aortic aneurysms whenever possible.[12] The first patient, a 46-year-old Negro man with a syphilitic aneurysm of the innominate artery and adjacent aorta, was operated upon July 12, 1951 (Fig. 1). Approximately twenty-three months later there is no evidence of recurrence of the thoracic lesion (Fig. 2), although nineteen months after the first operation another aneurysm of the abdominal aorta was excised and the defect bridged with an aortic homograft. In describing the operation in this patient, we called attention to the leathery consistency of the aorta in syphilitic aortitis permitting satisfactory insertion of sutures and favorable conditions for subsequent healing. Our second patient, in whom a massive aneurysm of the ascending and transverse arch of the aorta was excised, died fourteen hours later of diffuse cerebral damage as a possible complication of anesthesia. Recently, in an admirable consideration of this problem, Bahnson[4] reported on eight patients with saccular aneurysms located in different regions of the aorta, in six of whom excision and aortorrhaphy were successfully accom-

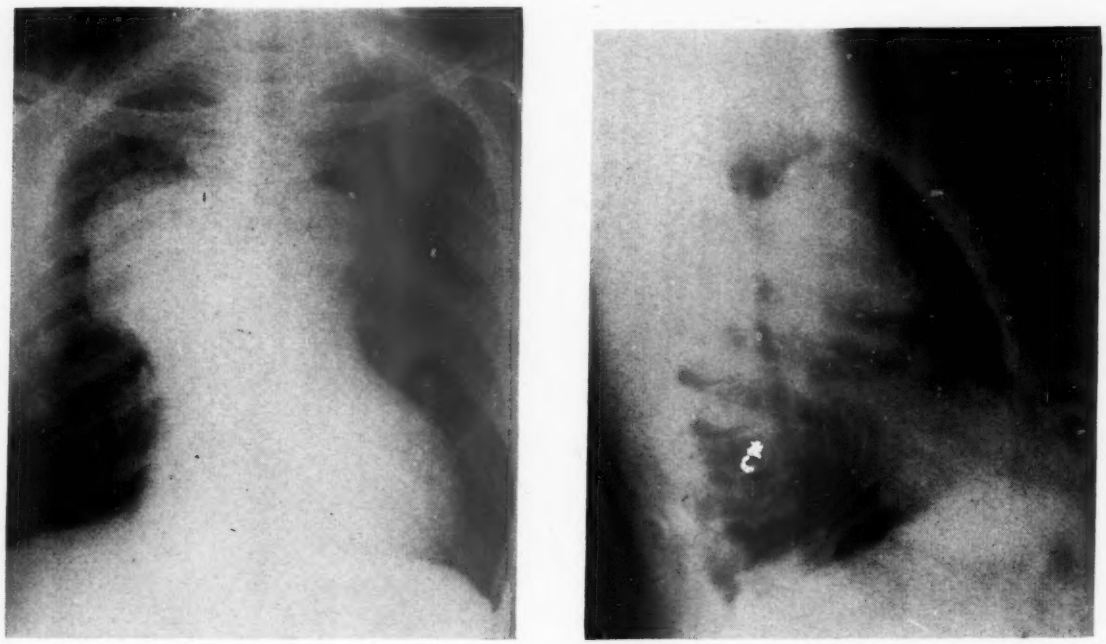
plished. On the basis of this experience he, like Tuffier[40] and us,[12] concluded that resection of saccular aneurysms is not only feasible but should be considered the procedure of choice in the majority of instances.

The choice of method of excision will vary according to the type of lesion, particularly as to whether it is sacciform or fusiform. In the former instance, continuity of the aorta may be preserved by tangential excision of the sac and suturing the defect in the aorta. Under these circumstances the aorta may not be involved in its entire circumference by the pathologic process, and sufficient normal tissue may be available for satisfactory repair of the defect. When excision of the sac makes it necessary to sacrifice a major tributary of the aortic arch, particularly the carotid arteries, ischemic changes may occur distal to the point of occlusion. Although restoration of continuity by arterial homograft may be desirable, this is seldom feasible, as evidenced by the fact that the recent case reported by Kirby and Johnson,[27] in which this was done, represents to our knowledge the only one of its kind. Because there is often some interference with blood flow through the carotid artery arising from such an aneurysm due to partial thrombosis or distortion, collateral blood supply to the brain may be sufficiently well established to permit safe ligation of the carotid artery. A preoperative test of carotid occlusion should always be made, although as shown by Kirby and Johnson this is not always a reliable index of adequate collateral blood flow. In their case of saccular aneurysm of the innominate artery, the preoperative occlusion test of the right common carotid artery for forty minutes did not provide reliable evidence that the patient could tolerate innominate artery occlusion for the period of fifty-seven minutes required to perform resection and anastomosis, as the patient developed partial paralysis of the left arm and leg. Since the test was performed immediately preceding the operation, it is possible, as they indicated, that this may have contributed to the decreased tolerance to innominate occlusion, suggesting that a greater interval of time, perhaps several days, should occur between the test and the operation.

For fusiform aneurysms of the aorta the problem is somewhat different, in that removal of the lesion will necessitate resection of an entire segment of the vessel. Restoration of continuity of the aortic flow must then be obtained by bridging the defect with an arterial homograft or a suitable plastic prosthesis. Resection of segments of the aortic arch has not been successfully accomplished. Although by using temporary shunts Schafer[37] was able to resect a portion of the thoracic aorta, the patient died shortly after completion of the operation. Perfection of suitable shunts, perhaps combined with hypothermia and artificial heart-lung apparatus, may make this procedure feasible. In lesions of the descending thoracic aorta it is possible to occlude the aorta for a short period of time without producing ischemic changes in the spinal cord or kidneys. We have occluded the lower thoracic aorta in two cases for periods of twenty-two and fifty-eight minutes without evidence of cord or renal damage, and Bahnson[4] has had a similar experience.

The technique of aneurysmectomy in sacciform aneurysms of the thoracic aorta consists primarily of careful mobilization of the neck of the aneurysm

in preparation for occlusion, following which a suitable clamp is applied to the neck of the lesion. The aneurysm is then completely mobilized from surrounding structures and excised, leaving a cuff of tissue in the clamp. The neck of the aneurysm may be sutured with a double row of interrupted 000 black silk sutures using a proximal row of mattress sutures and distal row of figure-of-eight sutures over the ends of the cuff. On removing the clamp there is usually some bleeding from needle holes, but this ceases spontaneously. In other instances, particularly where the lesion arises distal to the left subclavian artery, it may be desirable to occlude the aorta proximal and distal to the aneurysm for a short time as the aneurysm is excised and the aortic defect sutured by an open technique.



A. *B.*

Fig. 3.—(*A*) Anterior posterior and (*B*) lateral roentgenograms of chest showing large slightly lobulated aneurysm of ascending aorta.

Whereas the actual procedure of excision is fairly uniform in sacciform lesions of the thoracic aorta, the choice of approach must vary according to its exact location. For lesions involving the proximal aorta along the arch, an anterior thoracotomy incision perhaps provides the most satisfactory exposure, and additional exposure may be obtained by a midsternal extension cephalad or by crossing the sternum into the opposite pleural cavity. This may be illustrated by the method used in the case of an extensive syphilitic aneurysm of the ascending aorta in a 60-year-old Negro man (Fig. 3). This aneurysm was producing obstruction of the trachea, esophagus, and superior vena cava, and the patient was in acute distress. Adequate exposure of the aneurysm was obtained by a preliminary right anterior thoracotomy incision in the fourth intercostal space which was then extended as a median sternot-

omy (Fig. 4). The neck of the lesion was occluded with a noncrushing clamp, and the sac was excised leaving a cuff of tissue for sutures. The defect was closed with interrupted mattress sutures of 000 black silk and figure-of-eight sutures over the cut edges of the aorta (Fig. 5). The patient's obstructive symptoms were markedly relieved, and the roentgenogram (Fig. 6) of the chest ten days after operation showed striking alteration in the mediastinal shadow. He was preparing to leave the hospital on the fifteenth day after operation when he died suddenly. Autopsy revealed a spontaneous aortic perforation just above the sinus of Valsalva producing fatal pericardial tamponade. The site of the previous aortorrhaphy was intact and healing satisfactory.

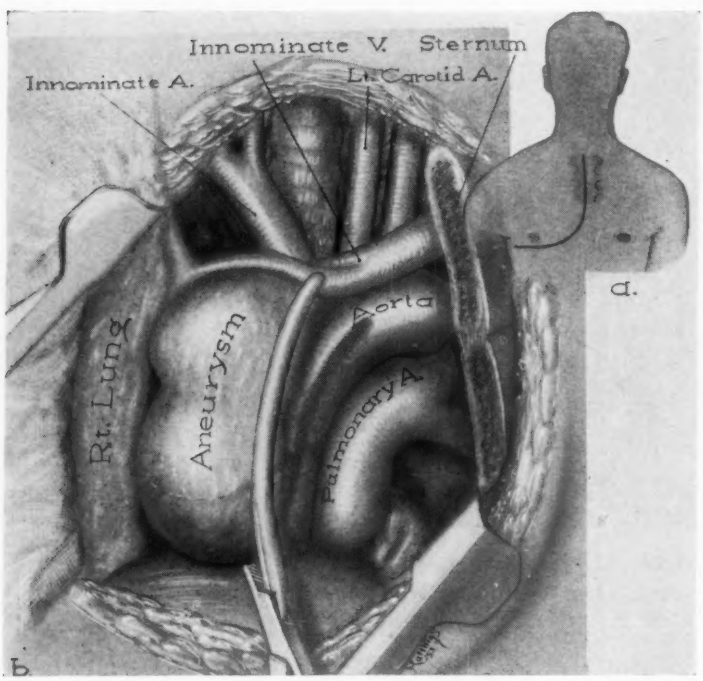


Fig. 4.

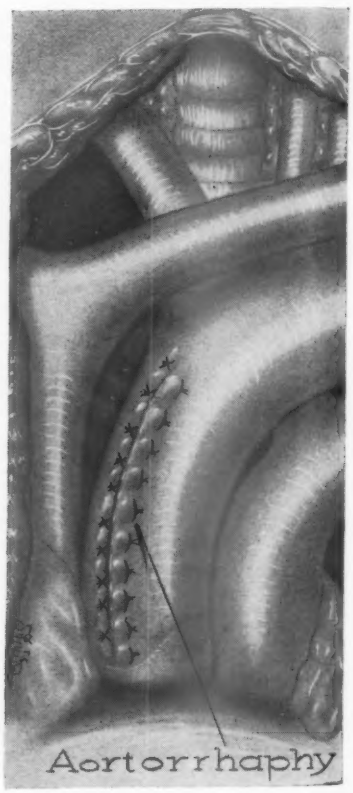


Fig. 5.

Fig. 4.—Drawing showing (*a*) operative approach employed for sacciform aneurysm of aorta in patient whose roentgenogram is shown in Fig. 3; (*b*) anatomic relationship of aneurysm and mobilization of neck for application of occluding clamp preliminary to excision.

Fig. 5.—Drawing showing excision of aneurysm and aortorrhaphy in case referred to in Fig. 4.

For lesions of the aortic arch we have employed an anterior thoracotomy incision initially entering the third or fourth intercostal space on the right or left side depending on the respective side of involvement. Additional exposure may then be obtained by extending the incision cephalad through the midline of the sternum or transsternally into the corresponding intercostal space on the opposite side. Lesions of the descending thoracic aorta are ex-

posed most satisfactorily by a standard posterolateral incision, removing an appropriate rib. This is illustrated by the operative procedure employed in a case of sacciform aneurysm of the descending thoracic aorta in a white man 56 years of age (Fig. 7). Thoracotomy through the bed of the resected left

Fig. 6.—Roentgenogram of chest of same patient as shown in Fig. 3 taken ten days after operation showing relative return to normal.

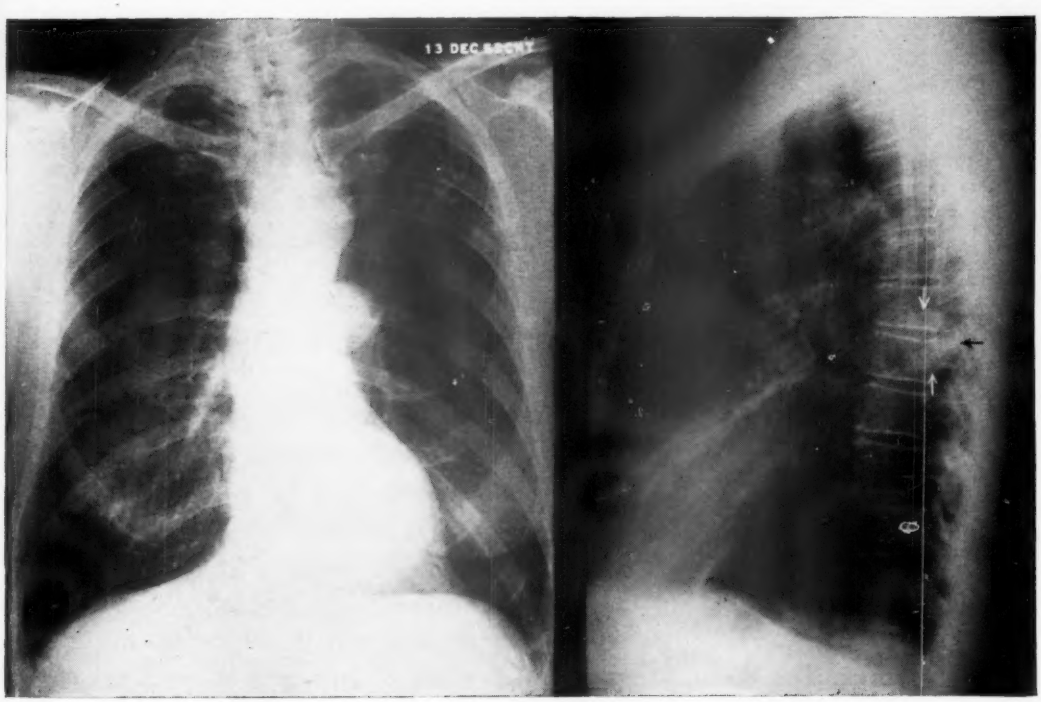


Fig. 7.—Anterior posterior and lateral roentgenograms of chest showing round posterior mediastinal shadow representing sacciform aneurysm of descending thoracic aorta.

eighth rib provided excellent exposure for tangential excision and aortorrhaphy (Fig. 8). Unfortunately, this patient expired two months later from a cerebrovascular accident, and autopsy revealed the aortic suture line to be well healed.

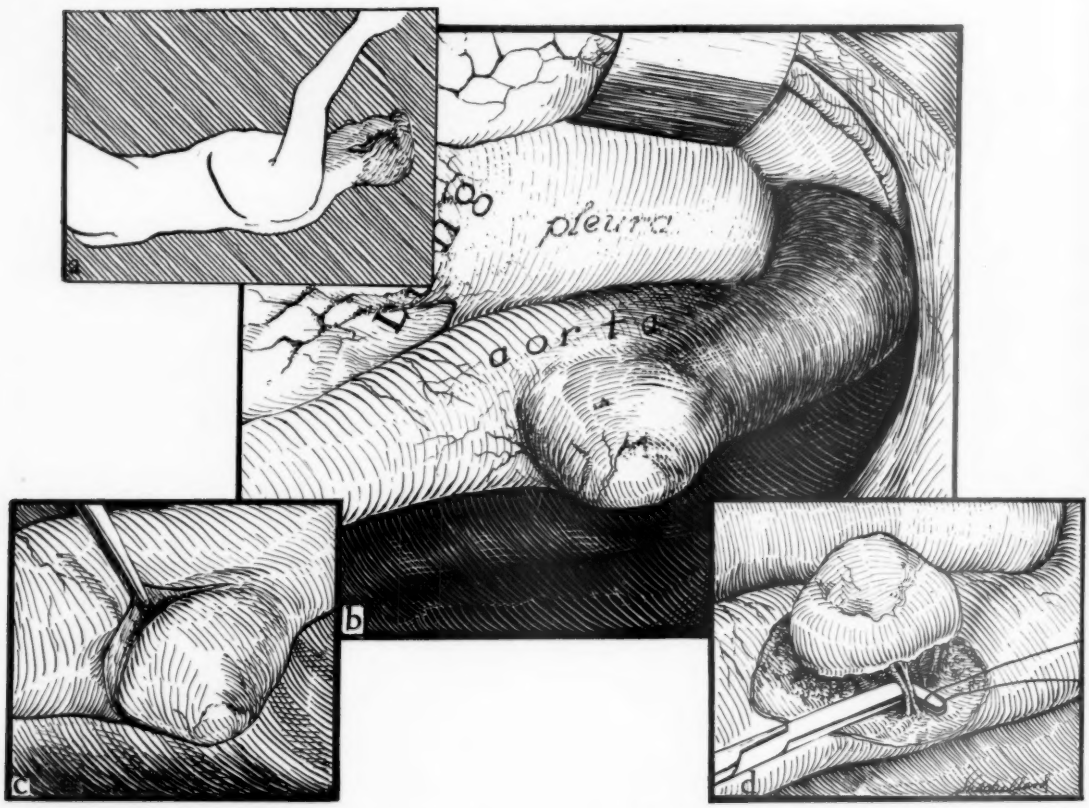


Fig. 8.—Drawing showing operative technique employed in the excision of aneurysm in patient referred to in Fig. 1. (*a*) Operative approach by left posterolateral thoracotomy through bed of resected eighth rib. (*b*) Anatomic relationship of sacciform aneurysm. (*c*), (*d*), and (*e*) Mobilization of neck of aneurysm. (*f*) Application of occluding clamp to neck of sac. (*g*) Excision of aneurysm and repair of resultant defect by figure-of-eight sutures of 000 arterial silk placed in cuff distal to clamp. (*h*) Mattress sutures placed proximal to clamp. (i) Aortorrhaphy completed.

Most aneurysms arising in the lower thoracic or abdominal aorta involve a considerable segment of the parent vessel. In the lower thoracic and upper abdominal portion of the aorta such aneurysms are often syphilitic in origin. Although they tend to be sacciform in type, they are usually quite large and incorporate so much of the aortic wall in the sac that no actual neck exists. Aneurysms arising in the lower abdominal aorta are usually arteriosclerotic in origin and fusiform in type so that the aorta throughout the length of the aneurysm constitutes an integral part of the sac. Only rarely would it be possible following excision of such aneurysms to repair the defect by lateral aortorrhaphy. The circumstances under which this might be done are illustrated by a case recently described by Bahnson,[4] who successfully performed the procedure for a large sacciform aneurysm, probably of syphilitic origin, in

the upper abdominal aorta, immediately opposite the origin of most of the visceral vessels of the aorta. This is obviously the logical procedure under these circumstances, since preservation of aortic continuity and normal blood flow in the region of these visceral vessels is essential. Most of the aneurysms encountered in this region, however, arise below the origin of these visceral vessels, particularly the renal arteries, and only a small proportion will occur

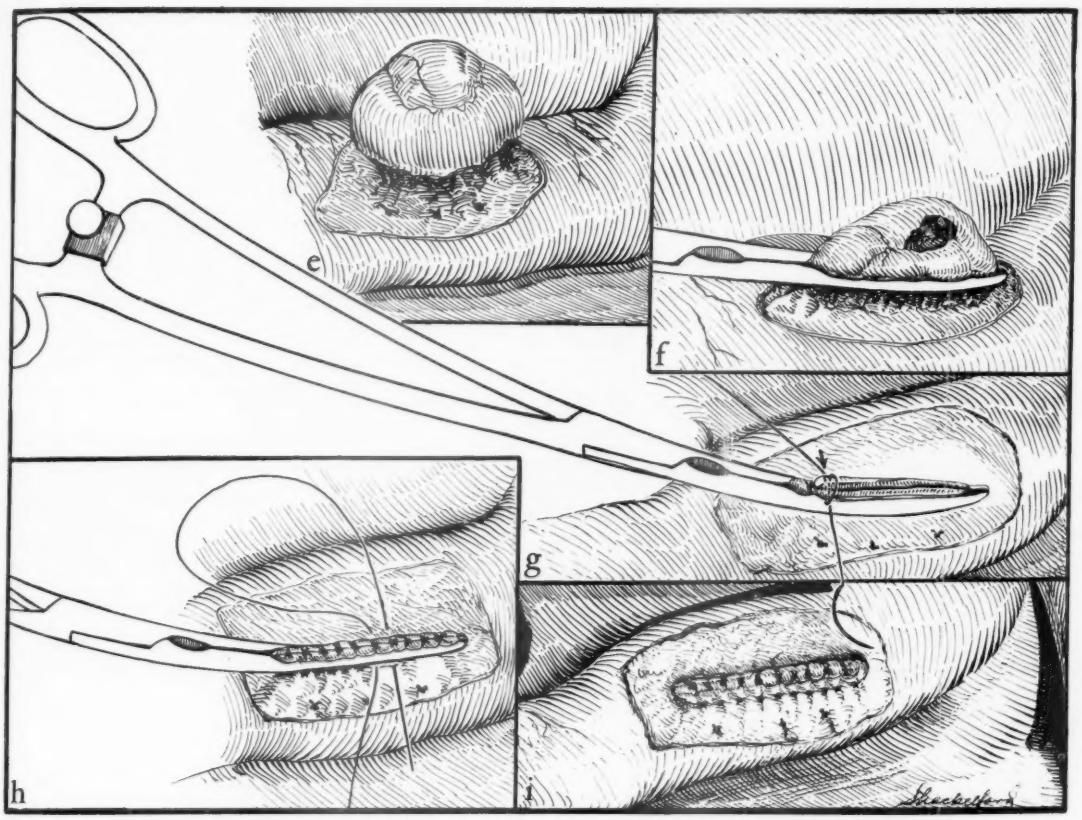


Fig. 8 *e-i.* (*For legend see opposite page.*)

immediately above them. Because of their characteristic extensive involvement of much of the aorta in the aneurysmal process, excision of the aneurysm necessitates creation of a defect in its continuity. This problem has been satisfactorily met by the use of aortic homografts to restore continuity of the aorta and normal blood flow. Evidence of the successful application of this procedure for aneurysms of the abdominal aorta has been recently provided by the case reported by Dubost and his associates[19] and that reported by Brock,[11] and for aneurysms of the lower thoracic aorta by that reported by us.[15]

Descriptions of the technical procedure that has been found satisfactory in our experience have been presented elsewhere.[15-17] and only the essential steps of the operation need consideration here. For aneurysms arising in the lower thoracic and upper abdominal aorta, adequate exposure may be obtained

by a left thoracoabdominal approach through the resected bed of the ninth or tenth rib with radical division of the diaphragm and mobilization of the visceral structures anteriorly and to the right. The aorta proximal and distal to the aneurysm is sufficiently mobilized and freed to permit the application of occluding clamps, following which the aneurysm and involved portion of the aorta between the clamps are excised. An aortic homograft of suitable length is used to bridge the defect in the aorta.

A midline abdominal approach is employed for aneurysms arising in the abdominal aorta below the renal arteries (Fig. 9). Exposure of the aneurysm is obtained by mobilizing the small intestine and its mesentery to the right and by linear division of the posterior peritoneal layer overlying the aneurysm along with the ligament of Treitz to permit mobilization of the duodenum to the right (Fig. 9). The aorta immediately above the aneurysm and below the renal vessels is then freed throughout its circumference and encircled with umbilical tape. The iliac arteries below the aneurysm are similarly treated, following which the aneurysm is freed from its surrounding structures, care being taken to avoid injury to the vena cava. Occluding clamps are then applied to the aorta above and the iliac arteries below, and the aneurysm is excised. An aortic homograft including the bifurcation, if this has been resected, is used to restore continuity (Fig. 10).

We have performed this procedure of resection of the aneurysm and involved aorta with replacement by aortic homografts in thirteen cases, in one of which the aneurysm was located in the lower thoracic aorta, in all the others arising below the renal arteries. In eleven of the cases the aneurysm was of arteriosclerotic origin, and in the other two it was probably syphilitic in origin, one occurring in the lower thoracic aorta and the other in the abdominal aorta. All but the latter two patients were over 60 years of age, and two were over 70 years. In all of the twelve cases in which the aneurysm occurred in the abdominal aorta it was fusiform in type, and in nine of these the aneurysm involved the bifurcation, necessitating its resection. In three of the latter the aneurysm had so extensively involved the internal iliac arteries that no distal portion remained for restoration of blood flow through them. In these cases the distal ends of aortic bifurcation homografts were anastomosed to the remaining external iliac arteries.

The only death in this series occurred on the thirteenth postoperative day of progressive uremia and secondary hemorrhage in a 74-year-old woman. Although the patient was recognized as a poor surgical risk because of severe impairment of renal and cardiac function, operation was advised and performed because of rapidly increasing symptoms and apparent imminence of rupture of the aneurysm.

The postoperative course in all the other patients was uncomplicated. Particularly significant is the fact that none manifested any evidence of ischemic changes as a result of the temporary occlusion of the aorta during the period of resection and anastomosis. Actually, the impression was obtained that the peripheral circulation was appreciably improved following operation. This is a noteworthy observation for it provides evidence to sug-

gest that for aneurysm in this region there is little or no need to consider the use of a temporary by-pass for blood flow during the period of temporary aortic occlusion, which in our cases averaged about one hour with the longest time being one hour and forty-five minutes.

Although this experience is relatively small and the follow-up period insufficient to provide final evaluation of the procedure, there is reason to believe from the early gratifying results in these cases and from certain experimental and other clinical uses of aortic homografts that this method of therapy constitutes the most satisfactory approach to such aneurysms.

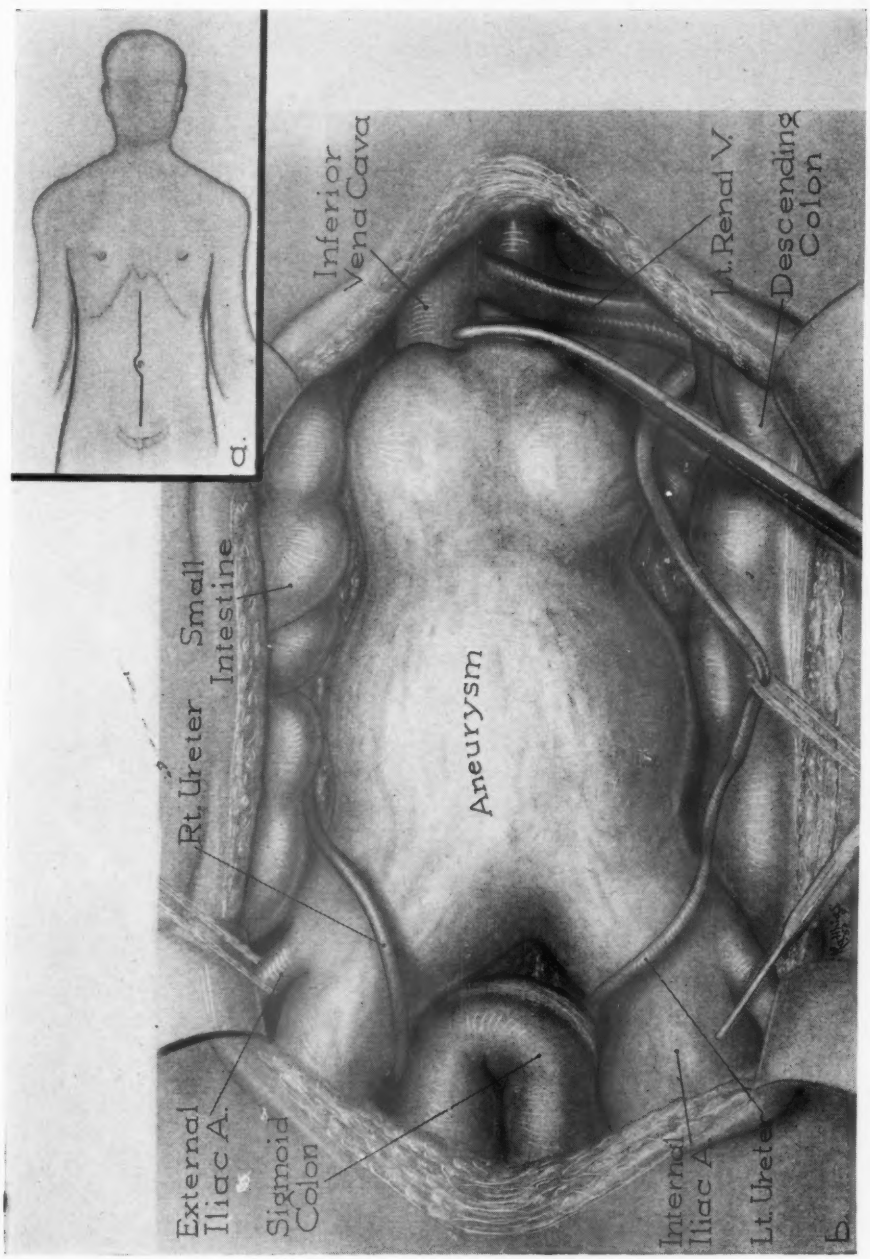


Fig. 9.—Drawing showing procedure used in excision of aneurysm of abdominal aorta involving both common and internal iliac arteries in a 60-year-old white man. (*a*) Midline incision for approach to aneurysm. (*b*) Anatomic relationship of aneurysm following its mobilization and exposure for application of occluding clamps to aorta above lesion and iliac vessels below.

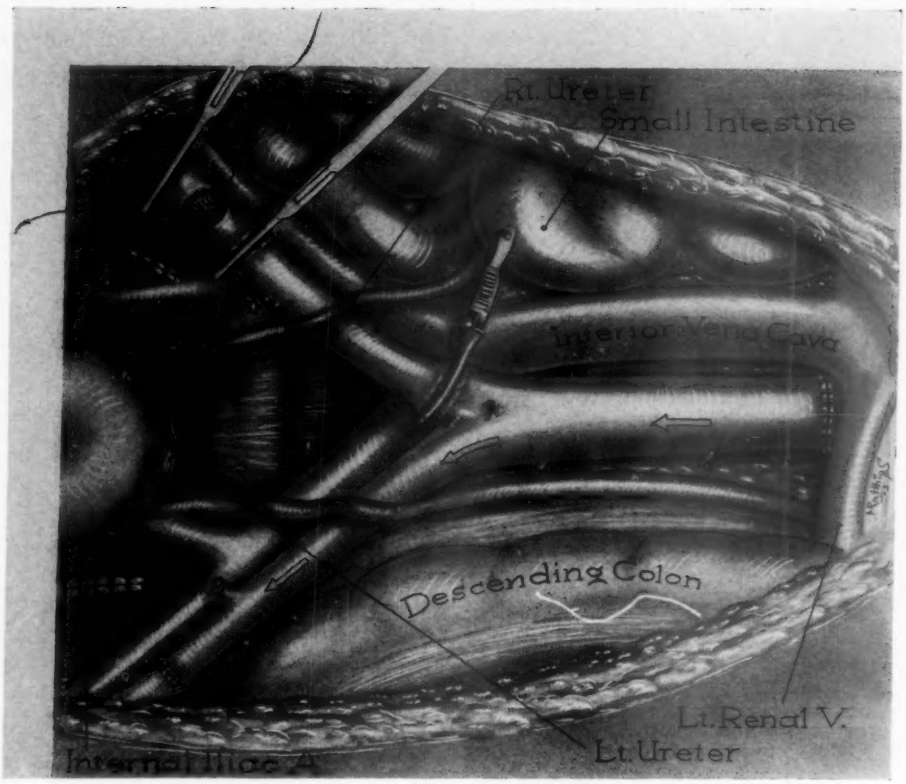


Fig. 10.—Drawing showing repair of defect by aortic homograft following removal of aneurysm in case referred to in Fig. 9. Because the aneurysm had destroyed internal iliac arteries, distal control of these vessels was obtained by endoaneurysmorrhaphy.

SUMMARY

1. Aneurysm of the aorta is a highly fatal disorder, emphasizing the need for prompt and definitive treatment.

2. The various methods of surgical treatment of aneurysms of the aorta have been directed toward obliteration of the aneurysm by promotion of thrombosis within the sac by ligation, introduction of foreign material, or stimulation of periarterial fibrosis. None of these methods has proved satisfactory, and only rarely has any of them achieved a cure.

3. Recent observations on patients with aneurysm of the abdominal aorta previously treated by cellophane wrapping and subsequently resected provide good reason to believe that this method not only has limited value but may even be harmful.

4. Excision of the aneurysm with restoration of continuity is considered the procedure of choice and may be applied much more frequently than has been previously realized. This can be accomplished in sacciform aneurysms of the thoracic aorta, usually syphilitic in origin, by tangential excision with lateral aortorrhaphy.

5. For aneurysms of the lower thoracic and particularly the abdominal aorta, most of which are fusiform and arteriosclerotic in origin, excision of

the aneurysm usually necessitates resection of a varying segment of the aorta. Under such circumstances restoration of aortic continuity requires the use of aortic homografts.

ADDENDUM

Since the presentation was made, excision of aneurysms of the aorta with restoration of vascular continuity by aortic homograft has been performed in fourteen additional patients. In eleven of these cases, the aneurysm involved the abdominal aorta and necessitated removal of the bifurcation. Three deaths have occurred in this latter group, two of which occurred during the first few days after operation as a result of coronary thrombosis and the third of which occurred more than one month later, presumably from pelvic thrombosis. All other patients surviving the operation, including those in the original report, remain well. In three more instances of aneurysm involving the thoracic aorta, the lesion has been resected and the aortic segment replaced by a homograft. Two of these were associated with coarctation of the aorta, and the third was an extensive syphilitic aneurysm in which the defect after excision extended from the level of the left subclavian artery to a point just above the diaphragm. The patient developed moderate weakness in the legs after operation, but he now walks unassisted and is otherwise asymptomatic.

Recently lyophilized or freeze-dried aortic homografts have been used almost exclusively for aortic replacement.

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RESECTION OF ANEURYSMS OF THE ABDOMINAL AORTA WITH ANASTOMOSIS OF THE SPLENIC TO THE LEFT ILIAC ARTERY

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THE surgical treatment of aneurysms of the abdominal aorta was chiefly obliterative in character until the past decade. In 1940, Elkin,[1] in his classic paper, reviewed all the cases previously reported since the first operation by Sir Astley Cooper in 1817 and reported his own case successfully treated by partial ligation. In his discussion he remarked that "it is improbable that wiring, coagulation or the application of the Matas principle of endo-aneurysmorrhaphy could be carried out without any great hope of success." During the past few years, advances in vascular surgery have permitted the treatment of aneurysms of the abdominal aorta to pass from the obliterative to the reconstructive or restorative stage. Prevention of further expansion by the application of cellophane,[2-6] cutis graft,[7] or external prosthetic devices[8, 9] has been one avenue of approach. Replacement of the segment of aorta by fresh or preserved aortic homografts[10-12] has been another method of attack. Two years ago, we[13] reported on the use of autogenous vein-inlay graft in the treatment of this condition. Follow-up study in two of these patients who recovered revealed the fact that thrombosis had taken place in one person. In the second case, although the patient is still free from symptoms thirty months after operation, the follow-up aortogram revealed considerable dilatation of the vein within the aneurysmal sac. The end results in these cases suggested that some other way might be found of handling this problem of anuerysmal dilatation of the abdominal aorta.

Arterial by-pass was first suggested for the treatment of arterial lesions by Blalock and Park.[14] By anastomosis of the left subclavian artery to the aorta in dogs, they suggested a method of treatment which might be used successfully in patients with coarctation of the aorta. The procedure has been occasionally used[15-17] in this condition where end-to-end approximation of the aorta could not be effected due to the long zone of narrowing. The use of the splenic artery to by-pass a long coarctation of the lower thoracic aorta has been reported.[18] An arterial shunt was also used by Lam and Aram[19] to by-pass a large aneurysm of the descending aorta.

In March, 1952, an aortogram of a patient who had a large abdominal aneurysm demonstrated the presence of a dilated, tortuous splenic artery. The abdominal aneurysm had been present for five years and had shown no signs of rupturing, but one month before admission the patient had developed gangrene of the left foot secondary to embolic occlusion of the posterior tibial artery.

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Since any obliterative procedure would probably have increased the ischemia of the left leg, it was decided to attempt to by-pass the aneurysm by anastomosis of the splenic to the left iliac artery. The operative procedure has previously been reported.[20] No attempt was made to excise the aneurysm, and collateral circulation was depended on to maintain the circulation across the pelvis to the right leg. The technical details of the method of suturing the splenic artery at its bifurcation to the left common iliac artery are shown in Fig. 1. In the postoperative period the circulation to the left leg improved with demarcation of the gangrenous process in the foot. The blood flow to the right leg appeared adequate. The patient, however, developed a subdiaphragmatic abscess, and finally the aneurysm ruptured at the point where the left iliac artery had been closed by a suture. A similar complication had taken place in the patient treated by Lam and Aram[19] when the aneurysm of the thoracic aorta had been left in place. Because of this catastrophe it was decided in the next case to resect the aneurysm after completion of the spleno-iliac anastomosis. This operation has been successfully performed in two cases.

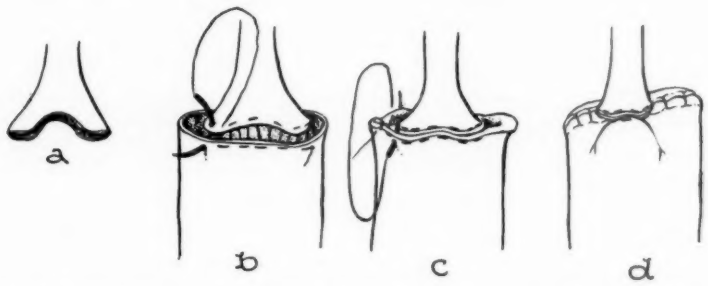

Fig. 1.—Method of anastomosis of splenic artery at its bifurcation to the left common iliac artery.

CASE 1.—M. R., a 57-year-old white woman, was admitted to the Franklin Hospital on May 8, 1952, with the chief complaints of pain in the back, a tender, pulsating mass in the epigastrium, and absence of pulsation of the femoral arteries. She had suffered from back pain for three years. One year before admission x-ray pictures had demonstrated dilatation of the abdominal aorta, but at that time the femoral and ankle pulses were normally present. Blood pressure readings had been consistently in the region of 120 to 130 systolic. In May, 1952, the systolic blood pressure suddenly rose to 200, pulsations of the femoral arteries disappeared, and there was impairment of circulation in both legs. On admission a tender, pulsating mass 9 cm. in diameter was present to the left of the umbilicus. Aortography (see Fig. 2) demonstrated complete occlusion of the abdominal aorta below the celiac axis. The right femoral artery filled through collateral vessels. Although the renal arteries were not visualized, the kidneys were outlined by the Diodrast. The urine showed a 2+ albumin, but the specific gravity was 1.022. Since the patient was able to excrete the Diodrast quite well, it was considered that she had fairly good renal function. The splenic artery was well visualized and appeared to be moderately dilated and tortuous.

Operation.—The patient underwent surgery on May 13, 1952. Under endotracheal anesthesia, a left thoracoabdominal incision was made through the eighth intercostal space. The abdominal incision was carried down as a left paramedian incision to the pubis; the diaphragm was divided along the line of the incision. The insertion of the left rectus was detached from the pubis, and the descending colon and sigmoid were reflected medially to expose the left iliac arteries and the terminal aorta. The left common iliac was found to be completely occluded by a firm thrombus; the tissues about the artery showed evidence of

inflammation, indicating recent thrombosis. The aorta just above the bifurcation was the site of a fusiform aneurysm which measured 12 by 8 cm. Expansile pulsation was present, but the aneurysm felt solid with calcareous plaques in the wall; it was adherent to the surrounding structures. The spleen was removed after dividing the vessels at the hilus, and the splenic artery was dissected free to the celiac axis. The superior surface of the pancreas was divided over a short distance to expose the origin of the splenic artery; the aorta at the diaphragm was exposed and, by digital dissection, a large tube was passed about this structure. The celiac axis pulsated vigorously. Although pulsation was present in the superior mesenteric artery, it was faint, and the pressure was low. After the nerves and lymphatics at the root of the superior mesenteric artery were divided, the aorta was again exposed and surrounded by a second rubber tube just below the celiac axis. The left common iliac artery was then divided at its origin. By digital pressure it was possible to express the thrombus from the left common iliac artery together with an atheromatous plaque. Good back-bleeding was then obtained from both the internal and external iliac arteries. A

Fig. 2.—Aortogram in Case 1 to illustrate obstruction of abdominal aorta below the celiac axis with filling of the right femoral artery through collaterals. (From Freeman and Leeds.[20])

polyethylene tube was inserted into the left external iliac artery for the intra-arterial administration of 5 mg. per cent heparin solution. The left common iliac artery was then brought beneath the left ureter, and an end-to-end anastomosis with the splenic artery was performed using a continuous intima-everting mattress suture. The polyethylene tube was then inserted into the splenic artery through an 18 gauge needle, and a continuous intra-arterial injection of heparin solution was maintained for the rest of the operation. On release of the occluding clamps, excellent pulsation took place in the common iliac artery below the line of anastomosis. The left renal vein was then dissected free, its branches were divided, and the aorta was exposed just above the aneurysm. The renal vein was quite dark, and the blood flow through this vessel appeared to be markedly reduced. There were three

renal arteries, and one of these was tortuous and pulsated vigorously. The largest one appeared to be solidly thrombosed. The right renal artery was never clearly visualized. The right common iliac artery was surrounded by a segment of rubber tubing and was found to be occluded by a thrombus. It was divided and both ends were sutured. The tube about the aorta below the celiac axis was then used to occlude the abdominal aorta while the aneurysm was resected. The duodenum was adherent to its anterior surface and had to be freed up by sharp dissection. Posteriorly, the aneurysm was found to be densely adherent to the vertebral bodies. With a curette a small thrombus was removed from the orifice of the right renal artery. The lining of the aorta as far as the orifice of the superior mesenteric artery was removed with a curette; it was possible to visualize the orifices of the left renal arteries. The lumen was irrigated with heparin solution and the aorta closed below the renal arteries with three interrupted figure-of-eight stitches of double-60 cotton together with a running stitch of 00000 Deknatel. At the conclusion of the procedure, although the left kidney was still cyanotic, a fair blood flow was demonstrable in the left renal vein. Penrose drains were placed in the pelvis and below the diaphragm. The polyethylene tubing which had been inserted into the splenic artery was brought out through the abdominal wall for the intra-arterial injection of heparin solution. At the conclusion of the procedure, the left femoral pulse was present and circulation to the right leg appeared adequate.

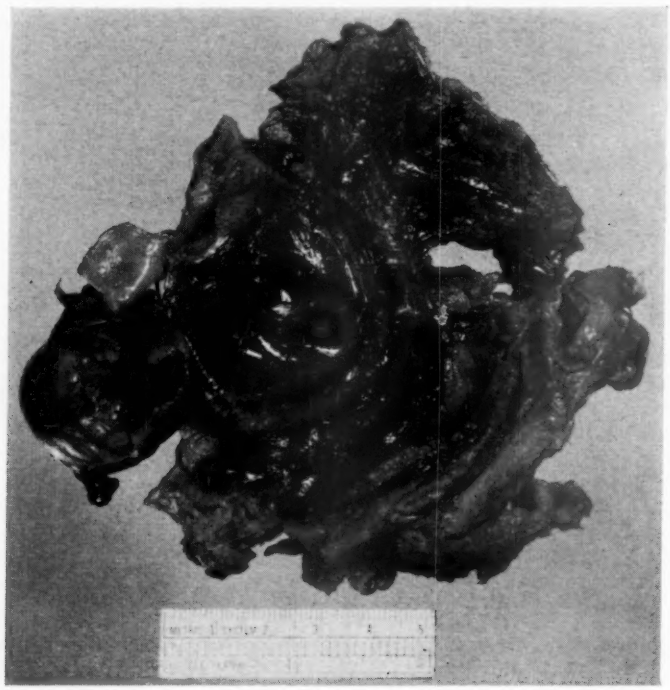

Fig. 3.—Aneurysm of bifurcation of abdominal aorta which has been opened to demonstrate the old organized thrombus and the fresh clot.

Pathologic Diagnosis.—Atherosclerotic aneurysm of abdominal aorta. When the aneurysm was opened (see Fig. 3) it was found to be occluded by a combination of old, partially organized thrombus with a fresher, nonorganized blood clot.

Postoperative Course.—The patient's postoperative course was remarkably good for the first six days, although there was a leukocytosis of 28,000 with 96 per cent polymorphonuclear cells. When the polyethylene tube, which had been inserted into the splenic artery, was removed she developed a retroperitoneal hemorrhage. On exploration the bleeding was found to come from a perforation in the splenic artery where the polyethylene tube had been

inserted. This laceration was closed with a suture of 00000 Deknatel. Four days later profuse chylous drainage developed from the wound. Cultures showed a hemolytic *Staphylococcus aureus* sensitive only to bacitracin and Chloromycetin. With local instillation of bacitracin, the infection gradually became controlled. The chylous drainage ceased, and the patient was discharged from the hospital on the forty-fourth postoperative day.

When examined eight months after operation, she was free from all abdominal and back pain and was able to walk as far as four blocks. Both femoral pulses were palpable, although weaker on the right side. The left dorsalis pedis was present. Oscillometry showed detectable pulsations at 80 mm. Hg on the right side. The excursion was ½ unit at 100 mm. on the left side. There was no blanching of the feet on elevation; pulsation of the splenic artery could be felt at the level of the umbilicus.

Fig. 4.—Aortogram in Case 1 to show rupture of spleno-iliac anastomosis eleven months after operation.

Subsequent Course.—The patient was readmitted to the Franklin Hospital on April 22, 1953, because of recurrence of pain in the left sacroiliac and gluteal regions, radiating down the left thigh, of two weeks' duration. Examination revealed a tender, pulsating mass in the left side of the abdomen. The blood pressure was 230/110. A faint pulse could be felt at each femoral area, but no pulses were palpable at the ankles. Oscillometry showed a ¾ unit deflection at 60 mm. Hg on the right and 1½ units of excursion at 80 mm. Hg on the left side. Reactive hyperemia test showed a filling of the vessels in the left foot at 65 cm. above the right auricle and at 60 cm. on the right side. Aortography (see Fig. 4) demonstrated a rupture of the spleno-iliac anastomosis. Although there was good filling of the right renal artery, the left renal artery was not visualized. The left iliac artery filled by way of the splenic artery, but on the right side, as before the initial operation, the circulation was maintained through collaterals.

Operation.—The patient underwent surgery on April 28. The splenic artery was readily exposed just below the ligament of Treitz. Although pulsation was present, the

pressure measured with a manometer was only 44 mm. Hg. A pulsating hematoma was present behind the sigmoid flexure. After control of the component vessels, as shown in Fig. 5, the left common iliac artery was opened at its bifurcation where it was found to be the site of aneurysmal dilatation. The splenic artery was opened just above the previous

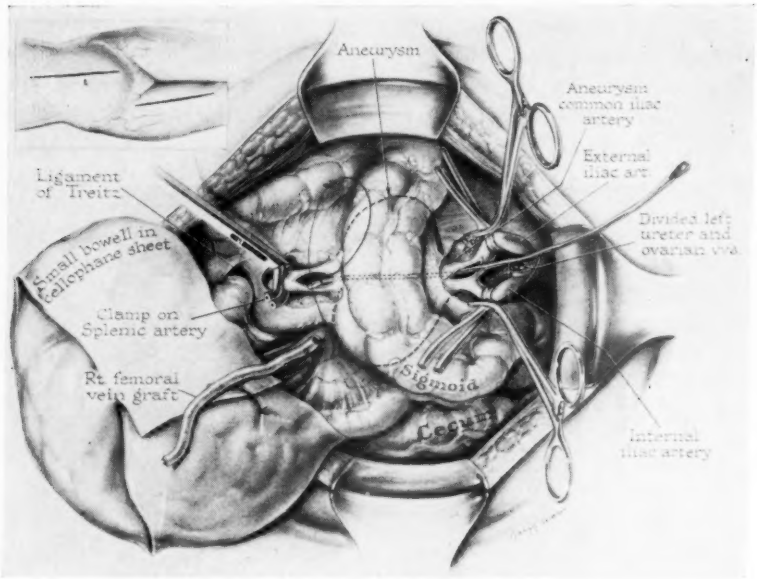

Fig. 5.—Drawing made at the time of the third operation in Case 1 to illustrate probe passed up from the left common iliac artery to the splenic artery preparatory to drawing the vein graft down into place.

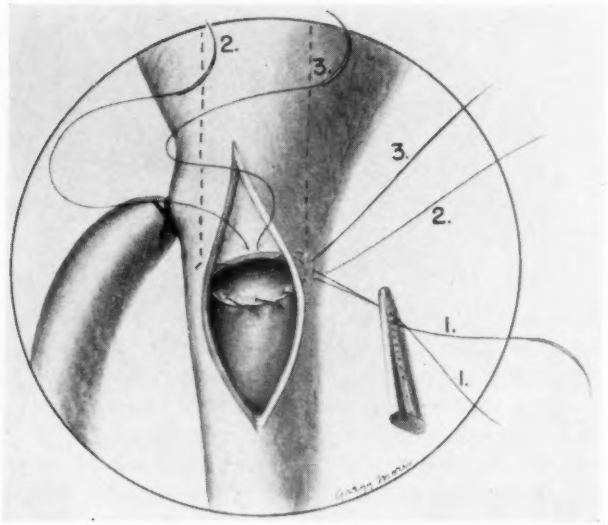

Fig. 6.—Technique of intraluminal suture of vein-inlay graft .

anastomosis. A malleable probe was then passed up from the common iliac artery through the hematoma to the splenic artery, and a segment of the patient's right superficial femoral vein was drawn through the gap between the splenic artery and the left external iliac artery. This vein was sutured into the lumen of the vessels by the technique illustrated in Fig. 6, and

the arteries were closed. On release of the clamps, pulsation was palpable in the left external iliac artery. Because of previous complications from intra-arterial heparin, it was decided not to insert a polyethylene tube into the splenic artery.

Postoperative Course.—The patient was placed on an oscillating bed, and intermittent administration of heparin commenced the day after operation. A faint femoral pulse was palpable on the right side but there was none on the left. The left foot showed considerable ischemia but there was no loss of sensation. Two weeks after operation, oscillometry showed no pulsations on the left side and a ¼ unit deflection at 80 mm. Hg on the right side. Reactive hyperemia test showed filling on the right side at 65 cm. above heart level, but on the left side filling was not complete until the foot was lowered to 15 cm. above heart level. Aortography showed thrombosis of the vein-inlay graft. Both femoral arteries filled by way of collaterals. The patient was discharged on the eighteenth postoperative day.

Fig. 7.—Preoperative aortogram in Case 2 to show large abdominal aneurysm involving the bifurcation extending from just below the renal arteries to the bifurcation.

She was admitted to another hospital because of nausea and vomiting and was found to have impairment of renal function. Blood creatinine was 9.3 mg. per cent. Improvement gradually took place, the creatinine went down to 3.8, and she was discharged to her home. She has since become ambulatory, and although the circulation to the left lower extremity is still precarious, gradual improvement is taking place.

CASE 2.—L. B., a 54-year-old white man, was admitted to the Franklin Hospital on Jan. 4, 1953, with the chief complaint of a mass in the abdomen of one year's duration. The mass was not painful but he was aware of the pulsation, especially when lying on his back. There was no history of intermittent claudication or coldness of the lower extremities. Six weeks before admission a gastrectomy had been performed for a chronic duodenal ulcer with obstruction which had not responded to medical management. At the time of operation exploration revealed a large, fusiform aneurysm involving the bifurcation of the abdominal aorta.

Physical examination revealed a well-developed person who appeared slightly older than his stated years. Blood pressure was 150/100. Urinalysis showed a trace of albumin, and the blood count was within normal limits. Both femoral pulses were dilated, the left side more than the right. The dorsalis pedis and posterior tibial ankle pulses were readily palpable. Preoperative aortography (Fig. 7) showed a fusiform aneurysm of the abdominal aorta originating just below the renal arteries. The iliac arteries appeared to be dilated and tortuous. The splenic artery was long and tortuous but appeared to contain no calcified plaques.

Fig. 8.—Gross specimen of Case 2.

Operation.—The patient underwent surgery on Jan. 6, 1953. Under endotracheal anesthesia, a left thoracolumbar incision was made through the eighth intercostal space, continued as a left paramedian incision. The abdomen was remarkably free from adhesions. The gastric anastomosis was in excellent condition. The spleen was removed and the splenic artery dissected back to the celiac axis, dividing and ligating its branches with No. 60 cotton. The splenic flexure and descending colon were then reflected medially, the anterior surface of the left kidney was exposed, and the left renal vein was followed to the aorta. At this point the aneurysm was found to arise just below the renal vein and was surrounded by a considerable amount of edematous tissue. The lymphatics and veins on the anterior and left lateral side of the aorta were divided and ligated, and by finger dissection, a rubber tube was placed about the aorta below the renal vein. The descending colon and sigmoid were reflected medially and the aorta was exposed retroperitoneally to its bifurcation. The ureter and spermatic vessels were allowed to fall posteriorly. Both iliac arteries were markedly tortuous. The right iliac had a firm, sclerotic plaque on the posterior wall, and there was a smaller plaque in the left common iliac. Both iliac arteries were dissected free to their bifurcations, and the aorta was then freed up by dividing and ligating the transverse lumbar, middle sacral, and inferior mesenteric arteries. The right common iliac artery was then clamped and divided, and its proximal end was closed with a running stitch. The distal end was irrigated with heparin solution. The sclerotic plaque in the posterior wall was removed. A Potts clamp was applied to the left iliac artery, and an end-to-side anastomosis of the right to the left common iliac artery was performed. There was some difficulty with this

anastomosis since the right iliac artery was friable where the sclerotic plaque had been removed. The left common iliac artery was then clamped and divided, and the aorta was occluded just below the renal arteries. The distal end of the splenic artery was anastomosed to the left common iliac artery. A posterior row of intima-everting mattress sutures were first inserted with stay sutures at the two angles and an over-and-over stitch on the anterior surface. Before completion of the anastomosis, a large fresh thrombus was expressed from the left iliac artery. Good back-bleeding was then obtained from both iliac arteries. At the completion of the anastomosis, after release of the clamps, pulsation was present below the suture line and a pulse was palpable in both common iliac arteries. A thrill could be felt opposite the anastomosis of the right iliac artery. The aneurysm was then excised and the aorta below the renal arteries closed by a running stitch of doubled No. 60 cotton. The patient withstood the operation in good condition, and at the conclusion of the procedure both feet were of normal color and pulses were palpable at each groin.

Pathologic Diagnosis.—Pathologic diagnosis was atherosclerotic aneurysm of the abdominal aorta (see Fig. 8). Sections through the aneurysm showed complete destruction of the usual architecture with no distinction between the intima and the media.

Fig. 9.—Postoperative aortogram in Case 2 to demonstrate the filling of the iliac arteries through the transposed splenic artery.

Postoperative Course.—The patient's postoperative course was quite smooth until the third day when he developed partial atelectasis of the right lung which was treated by endotracheal suction. Gastric suction was continued for three days. Ankle pulses could not be felt until the fifth postoperative day. Studies in the Vascular Research Laboratory two weeks after operation showed filling of the smaller blood vessels of both feet at 45 cm. above heart level. Oscillometric readings at the thighs showed a barely perceptible pulsation at 70 mm. Hg. Aortography (see Fig. 9) showed that both iliac arteries filled through the splenic by-pass.

When examined four months after operation, the patient still had some weakness in the legs after walking one mile on the level. Reactive hyperemia test demonstrated complete

filling of the left side at 45 cm., but there was some blanching of the right fifth toe which persisted until the patient sat up with the feet dependent. The dorsalis pedis and posterior tibial pulses were readily palpable at both ankles.

Discussion.—The splenic artery is an ideal vessel to be used as an arterial by-pass since it supplies an organ which can be removed with little or no serious consequences. It arises from one of the major divisions of the aorta, just below the diaphragm, and has but few small branches before its termination in the hilus of the spleen. Here it generally bifurcates, and this bifurcation can be used to provide a wider lumen at the point of anastomosis. A similar method has been described by Albanese,[21] by Johnson and Kirby,[22] and by Holman and Hahn.[23] The fact that the splenic artery is generally tortuous suggests that it has also become dilated.[24] Degenerative changes frequently accompany dilatation of vessels, and calcification may be found in this artery which may preclude its use. The splenic artery is also thin-walled in comparison to the common iliac artery. The atrophic character of the wall probably accounted for the secondary hemorrhage which resulted in the first case when the polyethylene tube was removed six days after the first operation.

Whether it is possible for the splenic artery to carry a volume flow of blood sufficient to maintain the circulation to the pelvis and lower extremities is still a matter of doubt. At the time of the third operation on the first case, pressure measurements indicated that the volume flow through the splenic artery was relatively low. The thrombosis which occurred following the vein-inlay graft between the splenic and the left external iliac arteries might have been due in part to this reduced volume flow.

One of these patients had already developed collateral circulation to the lower extremities following thrombosis of the abdominal aneurysm. The aortogram performed after the spleno-iliac anastomosis demonstrated that the circulation to the right lower extremity was carried chiefly through collaterals. The aortogram following the failure of the vein-inlay graft, demonstrated that the circulation of the left leg was also maintained through collateral vessels. In the second patient, provision for circulation to the right lower extremity was made by anastomosing the right common iliac to the left common iliac just below the spleno-iliac anastomosis. This procedure was only technically possible due to the fact that this patient had dilated, tortuous, elongated iliac arteries, a condition not infrequently encountered in patients with aneurysms of the abdominal aorta. The degenerative character of the arterial wall, however, makes these anastomoses not only technically difficult but also precarious.

SUMMARY

Two cases are reported in which arteriosclerotic aneurysms of the abdominal aorta were resected with anastomosis of the splenic to the left iliac artery. In one patient the right iliac was also anastomosed to the left iliac artery. Both patients recovered, and the circulation to the lower extremities, although reduced, was adequate. In the first case, secondary rupture at the spleno-iliac

anastomosis occurred eleven months after operation. Recovery followed after an unsuccessful attempt to insert a vein-inlay graft. The circulation to the lower extremities was through collateral vessels.

CONCLUSION

Aneurysms of the abdominal aorta may be resected with the circulation to the pelvis and lower extremities maintained through a spleno-iliac arterial anastomosis. This procedure, although fraught with difficulties, may be a useful one in selected cases.

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TREATMENT OF ANEURYSMS WITH FOLLOW-UP STUDIES ON DICETYL PHOSPHATE

A Report of Thirty-six Cases

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IF ONE adheres to the definition that an aneurysm is a hollow tumor, space, or sac, filled with liquid or coagulated blood, or both, directly connected with the lumen of an artery, and developed in whole or in part at the expense of the arterial wall, then treatment should be directed toward the restoration of normal caliber and form of the involved artery and preservation of the dependent circulation.

Aneurysm of the thoracic and abdominal aorta and the major branches long has been considered a fatal condition. Over one-half of the patients reported on by Kampmeier[1] died within one month after admission to the hospital. Colt[2] found the average duration of life in saccular aneurysms of the abdominal aorta to be about one year after the appearance of symptoms. Estes,[3] in a study of 102 patients with abdominal aortic aneurysms, most of which were arteriosclerotic, reported only 67.0 per cent alive after one year, none after ten years.

Galen recognized the nature of aneurysm, but Antyllus, in the second century A.D., attempted treatment by isolating an aneurysm between ligatures and emptying its contents. Versalius and others indicated a knowledge of these tumors and their fatal sequelae. After Harvey demonstrated the blood circulation, the nature and pathologic concept of these pulsating tumors were better understood. Measures then were taken both medically and surgically to treat this entity. Those aneurysms which were accessible were treated by operative means. Those which involved the circulation necessary to life were left to medical measures vainly designed to arrest the progress of the disease and alleviate pain. This was accomplished by venesection, low caloric diets, and drugs intended to diminish blood flow and pressure.

Surgical treatment embraced refrigeration, compression, acupuncture, filipuncture, electropuncture, ligature above and below the sac, occlusion of the parent artery by compression or gradual constriction (Halsted clamps, rubber bands, compression graded clamps), and finally the radical operations which included incision of the sac (aneurysmotomy), extirpation of the sac (aneurysmectomy), plastic procedures within the sac[4] (endoaneurysmorrhaphy, obliterative, restorative, and constructive), and the use of venous and

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arterial grafts. Until World War I, all of these procedures were used either alone or in combination. The results of these procedures because of shock, sepsis, hemorrhage, and gangrene were appalling, particularly before the advent of aseptic technique. It must be noted, however, that the workers of the past century in this field deserve the highest merit for their foresight and courage, as they certainly worked under many disadvantages which do not exist today. It is to their inventiveness that we are indebted for many of the basic techniques and procedures used at present in aneurysm surgery.

In all reported cases of aortic aneurysm treated by ligation prior to 1920, the patient did not leave the hospital alive. Since that year, successful ligation of the abdominal aorta for aneurysm has been reported by Biggers,[5] Elkin,[6] Matas,[7] and others.[8]

Wiring of aneurysms, introduced by Moore[9] in 1864, and since modified by Colt[10] and Corradi,[11] was a new step. The surgeons hoped to circumvent, by this technique, the risk of trauma, hemorrhage, and sepsis, and at the same time produce a clot in the sac. This procedure soon fell into disrepute. In 1926, Reid's[12] report of forty patients treated thus did not include a single cure and included only five who were relieved. Blakemore[13] has revised this procedure and by his magnificent results has given it firm footing. At the present time, he not only reinforces the internal wall of the sac by wiring and electrocoagulation, but also reinforces the external aortic wall with reactive polythene containing dicetyl phosphate. He has further refined his technique by surrounding the aorta proximal to the sac with rubber bands encased in the plastic to impede blood flow through the aneurysmal sac. The procedure deserves special notice, since he reports no hemorrhage at the point of constriction.

Today's surgeon, armed with clinically effective bacteriostatic agents, blood banks, advances in anesthesiology, familiarity with thoracic exploratory methods, advances in angiocardiography, and experience with grafting procedures and other blood vessel techniques, has increased the measure of relief and cure rate of aneurysm. He now calls upon a broader experience, and more wisely selects techniques not prejudiced by period or province but guided by the peculiarities of the lesion as it is exposed at the operating theater.

TABLE I. ANEURYSMS STUDIED (THIRTY-SIX)

LOCATION	NUMBER	LIVING	DEAD	RUPTURE
Thoracic aorta	13	4	9	3 (4)†
Abdominal aorta	14	7	7	4
Thoracoabdominal	1	1	0	0
Great vessels	8	5	3	0
Total	36	17*	19	8

*Survival periods: ten to eighteen months, eight patients; thirty-six to forty-two months, eight patients; six years, one patient.

†Rupture in thoracic aorta, three. The fourth was a wrapped abdominal aneurysm which seven months later ruptured above diaphragm into esophagus.

During the past six years, we have treated thirty-six aneurysms, altering the treatment to the patient's individual needs (Table I). We wrapped,[14] excised and wrapped, and simply excised aneurysms as conditions warranted.

Early in our experience, we chose to excise the aneurysmal sac whenever possible, and enveloped the reconstructed artery in polythene film containing dicetyl phosphate. It was only in extremely poor operative risks and in cases when extent of the arterial damage rendered the case inoperable that we wrapped only.

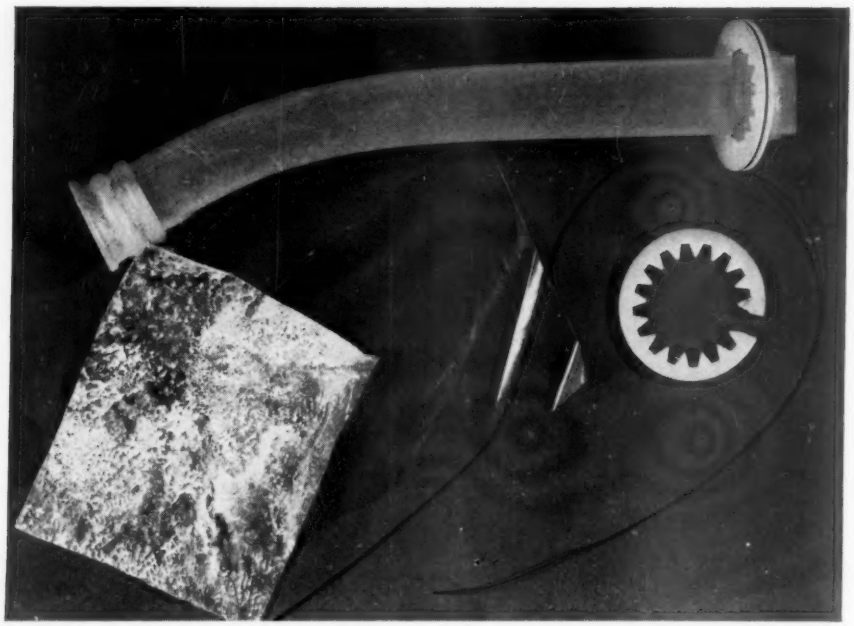

Fig. 1.—A sheet of polythene impregnated with dicetyl phosphate powder is in the lower left-hand corner. Compare with sheet of polythene containing less than 1 per cent dicetyl phosphate to the right. Both have been sterilized by boiling ten minutes in water. Immediately above is a pure polythene tube of the type used in Case 24. It is eight inches in length and three-fourths inch in internal diameter. Note the flare on the proximal end. The tube is fixed in the vessel wall after the method of Hufnagel.

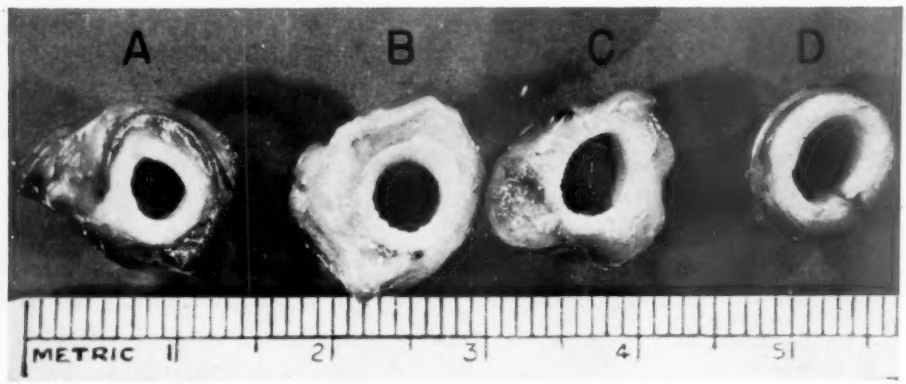

Fig. 2.—Cross sections from the thoracic aortas of four dogs *A*, *B*, and *C* have been wrapped six weeks with polythene and dicetyl phosphate in various concentrations. *B* contains heavily impregnated dicetyl phosphate, *A* contains 5 per cent dicetyl phosphate, and *C* contains regular polythene film containing less than 1 per cent dicetyl phosphate. *D* is an unwrapped aorta. Note the extra thickness of the vessel walls as early as six weeks after wrapping.

We were careful to choose film that contained dicetyl phosphate. This we found in past work to be necessary to the fibrotic reinforcement of the vessel wall.[15] Incriminations cast at polythene as an effective cicatrix-inducing material are

the result of conclusions drawn from work done using pure polythene instead of polythene containing dicetyl phosphate. Repeated experimental studies have further substantiated our conviction that polythene containing dicetyl phosphate will induce fibrosis to an effective extent in aneurysm surgery.[16] It is to be emphasized that the polythene must be sterilized by boiling, aqueous zephiran chloride or formaldehyde, as the use of alcohol in high concentration reduces the reaction of polythene in tissues considerably. To guard against use of mitigated film and to fortify the film, we, at present, iron dicetyl phosphate powder into the polythene before sterilization.* The resultant fibroblastic reaction is marked even at six weeks (Figs. 1 and 2).

CASE REPORTS

CASE 1.—W. F., age 38; saccular aneurysm, aortic arch, and sternal erosion. Operation: isolation neck of sac and encirclement with polythene strips. Result: excellent. Patient living three years, five months after operation.[17]

CASE 2.—W. M., age 49; large fusiform aneurysm, ascending arch and descending aorta with marked tracheal compression. Operation: posterior mediastinal tracheotomy and polythene wrap of arch and descending aorta. Three weeks later, ascending aorta wrapped. Result: returned three months later for routine evaluation. Died forty-eight hours following bronchoscopy with rupture into esophagus.[18]

CASE 3.—W. F., age 52; large fusiform aneurysm, descending aorta. Operation: left lower lobectomy and polythene wrapping of aneurysm. Result: Ten days after operation, patient went into shock with recovery. Died three and one-half months after operation. Autopsy: rupture, with polythene strips not in apposition to aneurysm wall. It was felt that the first bleeding episode ten days postoperatively "floated" the strips off the vessel wall.

CASE 4.—W. M., age 67; fusiform aneurysm, descending aorta. Operation: polythene wrap. Result: patient alive and symptom-free two years, five months after operation.

CASE 5.—W. M., age 49; fusiform aneurysm, ascending aorta and innominate artery. Operation: complete polythene wrap of innominate artery and ascending aorta. Result: comatose, right hemiparesis. Died first postoperative day. Autopsy: thrombosis, left carotid artery.

CASE 6.—C. M., age 43; fusiform aneurysm, ascending, transverse aorta and innominate artery. Operation: polythene wrap of ascending aorta and innominate artery. Stellate ganglionectomy, right. Result: disoriented and blind postoperatively. Died thirty-six hours later. Autopsy: negative.

CASE 7.—W. M., age 59; fusiform aneurysm, abdominal aorta. Operation: polythene wrap. Rewrapped fourteen months later. Result: fourteen months following operation, the mass seemed larger and the aneurysm was rewrapped. Now works a full day. Alive three years, two months after operation.

CASE 8.—W. M., age 61; fusiform and saccular abdominal aortic aneurysm. Operation: polythene wrap. Result: eighteen months later patient returned for hemorrhoidectomy. Died six weeks later. Autopsy: retroperitoneal rupture. Microscopic study showed the adventitia of vessel under the polythene to have been replaced with a hyaline type of connective tissue.

*This is accomplished by sprinkling the dicetyl phosphate powder on both sides of a polythene sheet and then encasing it between two sheets of cellophane to prevent the polythene sheet from sticking to the iron and ironing surface. The sheets are then pressed together by a warm iron (115° C.) and left to cool. The cellophane sheets then strip away with ease, leaving the heavily impregnated sheet of polythene. We then sterilize the polythene sheet by boiling it ten minutes in water.

CASE 9.—W. M., age 59; fusiform aneurysm, abdominal aorta and right common iliac artery. Operation: polythene wrapping of abdominal aorta. Result: patient living two years, three months after operation. The mass is described as "stoney" hard with minimal pulsations.

CASE 10.—W. M., age 62; fusiform aneurysm, abdominal aorta. Operation: polythene wrap. Result: seven months after operation patient developed severe hematemesis and died. Autopsy: rupture of aorta into the esophagus above the diaphragm. The wrapped aneurysm appeared satisfactory with considerable surrounding scar tissue.

CASE 11.—W. F., age 69; saccular aneurysm, abdominal aorta. Operation: polythene wrap. Result: died on eighth postoperative day. Autopsy: rupture.

CASE 12.—W. M., age 49; fusiform aneurysm, innominate and right subclavian artery. Operation: complete wrapping of aneurysm with polythene. Stellate ganglionectomy. Result: died thirty-six hours following operation. Autopsy: negative.

Cases 6 and 12 both died shortly after operation with cerebral edema following a relatively simple operation. Did the stellate ganglionectomies produce this complication by dilatation of diseased cerebral vessel walls?

CASE 13.—W. M., age 64; fusiform aneurysm, abdominal aorta. Operation: polythene wrap. Result: died one year, three months after operation. Cause of death: senile degeneration.

CASE 14.—W. F., age 60; fusiform aneurysm, abdominal aorta. Operation: polythene wrap. Result: excellent. Still living two years after operation.

CASE 15.—W. M., age 60; fusiform aneurysm, abdominal aorta. Operation: polythene wrap. Result: excellent. Still living one and one-half years after operation.

CASE 16.—W. M., age 64; saccular aneurysm, abdominal aorta. Operation: polythene wrap. Result: died eight months after operation, cerebral hemorrhage.

CASE 17.—W. F., age 66; fusiform aneurysm, right carotid artery. Operation: complete polythene wrap. Result: excellent. Still living six years after operation.

CASE 18.—W. M., age 68; saccular aneurysm, innominate artery. Operation: complete polythene wrap. Result: died eight hours postoperatively. Cause of death: massive atelectasis, right.

CASE 19.—W. M., age 65; fusiform aneurysm, innominate and right common carotid artery. Operation: polythene wrap. Result: excellent. Alive three years, four months after operation.

CASE 20.—W. M., age 43; saccular aneurysm, right popliteal artery. Operation: encirclement above aneurysm with polythene and wrapping of sac. Result: excellent. No circulatory disturbance three years after operation.

CASE 21.—W. M., age 49; fusiform aneurysm, left common carotid artery. Operation: ligation at aorta and bifurcation of carotid artery with excision of sac. Result: excellent. Patient living three years after operation.

CASE 22.—W. M., age 59; huge saccular aneurysm, abdominal aorta. Operation: polythene wrap. Result: died two months postoperatively with retroperitoneal rupture.

CASE 23.—W. M., age 44; fusiform aneurysm, right carotid artery. Operation: complete polythene wrap. Two months later followed by excision of sac and rewrap. Result: excellent. After first wrap the aneurysm continued to grow. Two months later, reopened and reaction not present so polythene removed. Most of sac removed, continuity re-established and area rewrapped. Subsequent animal experiments showed the original polythene inert, and it is felt that the wrong type of polythene was used.

CASE 24.—C. F., age 34; saccular and fusiform aneurysm, descending aorta with bone erosion. Operation: aneurysmotomy with closure followed twenty-four hours later by excision of aneurysm and replacement of descending aorta with a polythene tube* (Fig. 3). Result: patient died eighteen hours later with acute coronary insufficiency. Autopsy: tube intact. No leakage or thrombosis.[19, 20]

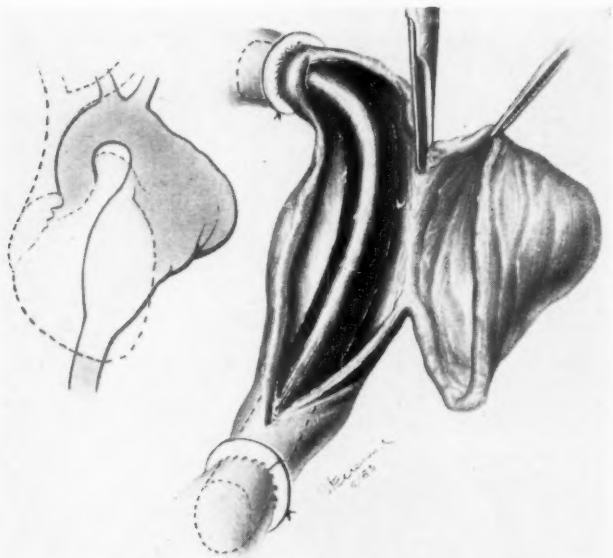

Fig. 3 (Case 24).—Shows the tube in situ and the blood flow re-established. Most of the sac was then cut away, intercostal vessels were ligated, and the remaining wall of the sac was approximated around the tube.

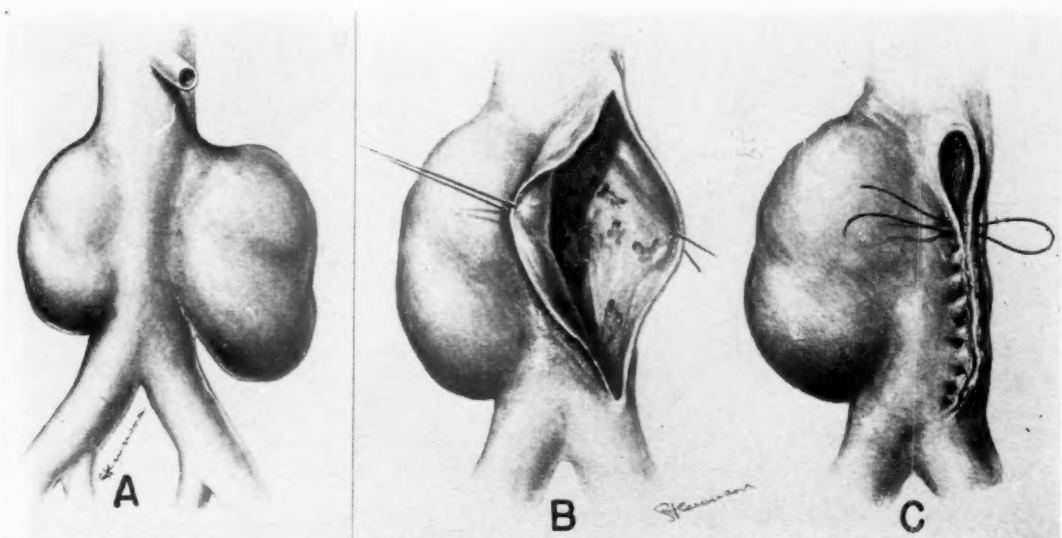

Fig. 4 (Case 32).—*A* shows large saccular aneurysm on left and fusosaccular aneurysm on right. *B* shows areas of ulceration and plaque formation inside sac. *C* shows method of closure. The repaired vessel was then wrapped with polythene.

CASE 25.—W. M., age 65; saccular aneurysm, left superficial femoral artery. Operation: ligation. Result: died eight hours postoperatively with acute dilatation of stomach and

*Acknowledgment is made to the National Plastic Products Company, Odenton, Md., which manufactured the pure polythene tube used in Case 24.

aspiration of vomitus. Autopsy: aspiration pneumonia but also fusiform aneurysm of the left subclavian and carotid arteries as well as the left common illiac artery.

CASE 26.—W. F., age 44; saccular and fusiform aneurysm of ascending and transverse arch of aorta. Operation: exploration with rupture into pericardium. Result: death by massive hemorrhage.

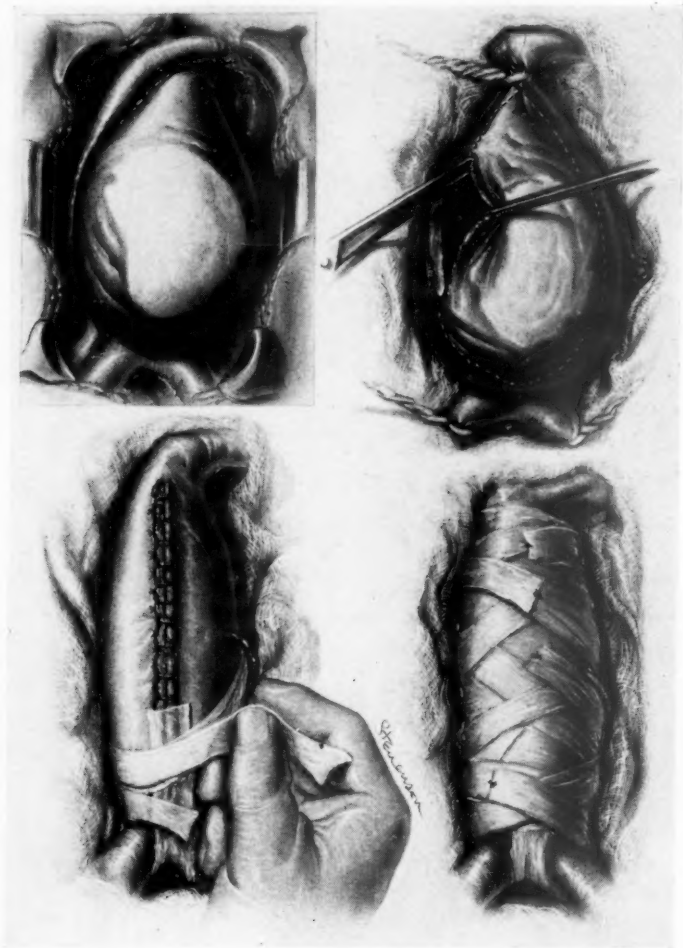

Fig. 5 (Case 32).—At exposure, note white anemic necrotic area in the aneurysm wall and also wrapping of the aneurysm with polythene after most of the sac has been excised.

CASE 27.—W. M., age 65; fusiform aneurysm, transverse and descending aorta. Operation: none. Result: ruptured into left pleural cavity while awaiting angiocardiography.

CASE 28.—C. F., age 42; saccular and fusiform aneurysm, transverse aorta. Operation: exploration with rupture and tear of aorta with repair and excision of sac. Result: death by cardiac arrest.

CASE 29.—W. M., age 62; fusiform aneurysm, abdominal aorta beginning 3 cm. above the right renal artery. Operation: polythene wrap. Result: died four days after operation. Autopsy: retroperitoneal hemorrhage with erosion of third lumbar vertebra.

CASE 30.—W. M., age 37; fusiform aneurysm, transverse and descending aorta. Operation: polythene wrap. Result: good. Still alive six months after operation.

CASE 31.—W. M., age 60; fusiform aneurysm, abdominal aorta. Operation: injection of dicetyl phosphate in oil[21] and polythene wrap. Result: good. Patient living six months after operation.

CASE 32.—C. M., age 60; left saccular aneurysm, abdominal aorta with daughter aneurysm on opposite side. Operation: excision of left sac wall and re-establishment of

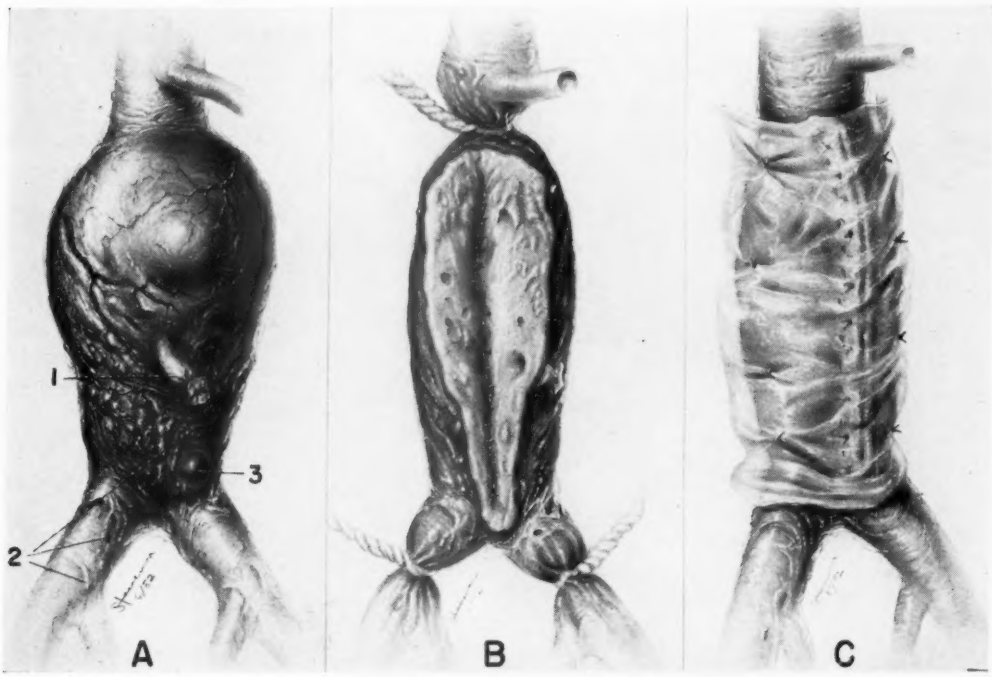

Fig. 6 (Case 33).—A fusiform aneurysm treated by partial excision, re-establishment of lumen, and polythene wrap. *1* shows ligated inferior mesenteric artery, *2* calcified plaques, *3* small daughter aneurysm.

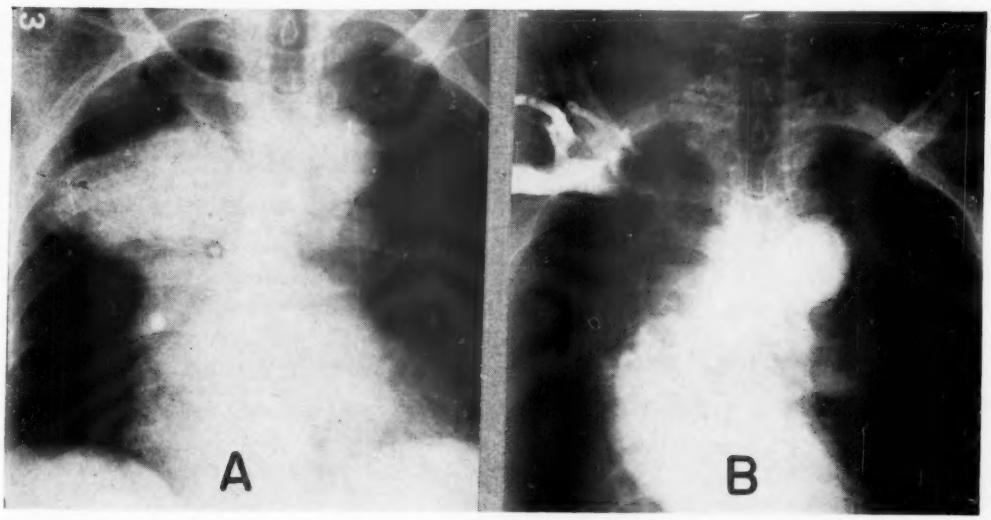

Fig. 7 (Case 35).—*A*, Retrograde aortagram showing catheter and contrast media in aneurysmal sac. *B*, Venous angiocardiogram three months after excision of sac.

lumen followed by polythene wrap (Figs. 4 and 5). Right saccular aneurysm clotted with good endothelial lining. Result: excellent. Alive and well one year, two months after operation.[22]

CASE 33.—W. M., age 66; fusiform aneurysm, abdominal aorta. Operation: longitudinal excision of diseased wall with re-establishment of lumen and followed by polythene wrap (Fig. 6). Result: excellent. Alive one year after operation.

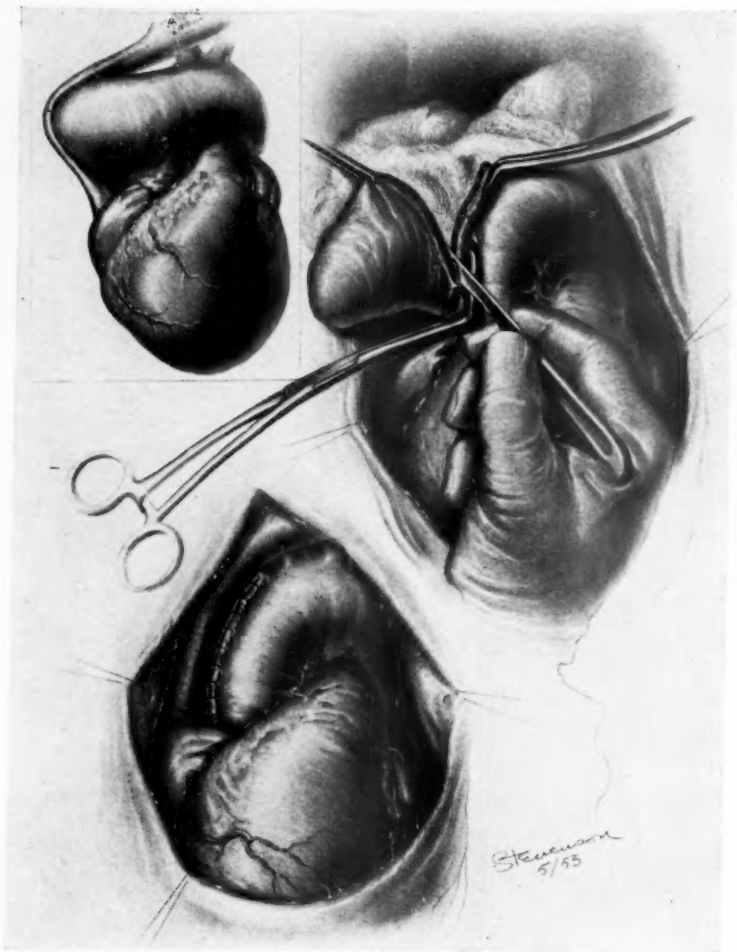

Fig. 8.—Technique used in re-establishing vessel continuity in Case 35. This case was not wrapped with polythene.

CASE 34.—C. M., age 66; fusiform aneurysm, descending aorta. Operation: double plication of aneurysm wall. Result: died thirty-six hours postoperatively. Autopsy: massive collapse of left lung. Cause of death, tension pneumothorax following plugging of thoracotomy drainage tube. (At operation a tear was made in the lung while dissecting it from the aneurysm wall.)

CASE 35.—C. M., age 60; saccular aneurysm, ascending aorta. Operation: excision of sac. Result: excellent. Alive eight months after operation (Figs. 7 and 8).

CASE 36.—W. M., age 58; fusiform aneurysm, lower thoracic and upper abdominal aorta. Operation: polythene wrap. Result: excellent. Alive three years, two months after operation.

COMMENT

The principle of fibrosis is an acceptable approach to palliative therapy. Dicetyl phosphate in polythene or some other suitable vehicle has merit in the treatment of aneurysm. The majority of cases in this series were amenable only to a wrapping technique. Surgical excision or plastic procedures on the aneurysm wall were anatomically impossible in most instances.

All aneurysms in this series were explored, and all were treated even though at operation the outlook appeared futile. Seven of the thirty-six cases ruptured postoperatively at the aneurysm site. Other causes of death, in this series, are tabulated in Table II.*

TABLE II. CAUSE OF DEATH

Rupture (operative site)	7
Rupture (other)	1
Thrombosis of carotid artery	1
Cerebral edema	2
Senile degeneration	1
Cerebral hemorrhage	1
Massive atelectasis	1
Acute coronary insufficiency	1
Acute dilated stomach with aspiration vomitus	1
Tension pneumothorax	1
Hemorrhage at operation	1
Cardiac arrest	1
Total	19

SUMMARY

Methods of surgical treatment of aneurysm of the aorta and great vessels are briefly reviewed.

Treatment of this clinical entity with preservation of the distal circulation is a reality with improvement of blood vessel techniques.[23]

Reinforcement of the vessel wall from without or within, excision, grafting, or the use of an artificial prosthesis is determined by the condition of the aneurysm wall, its anatomic location, type, and configuration. Each aneurysm should be individualized with reference to the surgical procedure of choice.

Further experimental studies using polythene and dicetyl phosphate in greater concentrations, as well as methods of sterilization, are discussed.

Follow-up of thirty-six cases of aneurysm of the aorta and great vessels treated by surgery is presented.

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INTRA-ABDOMINAL ARTERIAL ANASTOMOSES

An Experimental Study

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INJURY to the hepatic artery, occurring in the course of biliary tract or gastric surgery, may result in fatal liver necrosis following ligation of the vessel to control hemorrhage. Aneurysms of the hepatic artery have been a cause of exsanguination. Direct extension of a benign or malignant neoplasm to the vicinity of the hepatic or superior mesenteric arteries has constituted a serious obstacle to the extension of radical tumor surgery. Compromise of the middle colic artery by injury or neoplasm has necessitated sacrifice of the transverse colon. Thrombotic or embolic occlusion of the origins of the superior mesenteric or renal arteries has frequently eventuated in death of the patient.

The problem common to all of these situations is the need to restore an adequate supply of oxygenated blood to the jeopardized organ promptly. The availability of expendable intra-abdominal arteries suggests their use for such contingencies. Preservation of the aortic origin of the splenic artery or a renal artery and anastomosis of the mobilized segment of vessel to the distal portion of the artery to an essential organ may meet this requirement. An experimental program was outlined to determine the efficacy of this approach.

EXPERIMENTAL METHOD

Large mongrel dogs were utilized, of either sex, ranging in weight from thirty-five to ninety pounds. Anesthesia was provided by the intravenous administration of a standard preparation of veterinarian Nembutal solution in dosage of 1 c.c. per five pounds of body weight, occasionally augmented by small additional increments of the same medication. The peritoneal cavity was entered through a liberal vertical midline incision.

Mobilization of the designated vessels was carried out in a standard manner. The arteries to be sacrificed were isolated at their origins, stripped of perivascular autonomic nerve fibers and other tissues, and divided between a ligature placed proximally and a bulldog seraphine clamp placed distally. The donor vessel was similarly mobilized, and divided between a proximal bulldog clamp and a distal ligature. The continuity of the proximal end of the donor vessel with the aorta was preserved, together with a length of artery sufficient to reach the distal end of the sacrificed vessel without tension. Construction of the anastomosis was facilitated by leaving a generous cuff protruding beyond the clamp on the vessel to the essential organ. The ends of

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both arteries were irrigated with saline solution prior to commencing the reconstruction. The individual variations in technique employed for the specific procedures will be described.

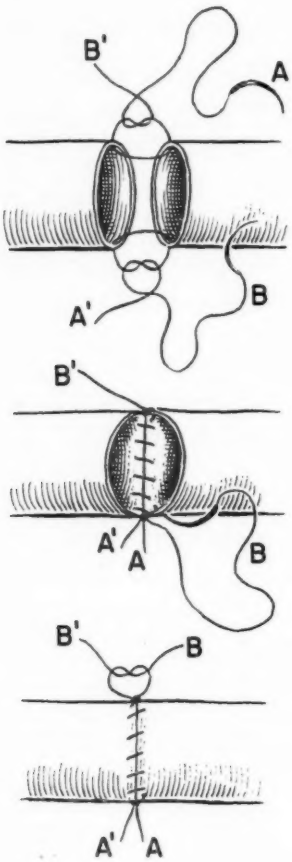


Fig. 1.—End-to-end anastomosis by continuous sutures, interrupted at lateral angles.

The initial arterial anastomoses were effected by using simple interrupted sutures of No. 00000 Deknatel braided silk on a curved, noncutting, atraumatic needle. As experience was acquired with the technical problems associated with the anastomosis of vessels averaging 3 mm. in outside diameter, and usually situated deeply within the abdomen, the construction of the suture line underwent many modifications. The technique employed in the later experiments, and eminently suitable for all of these procedures, involved the use of twelve-inch lengths of No. 00000 mild chromic catgut, armed at each end with a small, three-eighths circle, noncutting atraumatic needle.* The ends of the two vessels in question were aligned by two sutures, placed at the lateral angles. The use of suture material with a needle at each end permitted passing the needle from the intimal surface of each vessel out through the adventitia. When needles are passed from outside in, in such small ves-

*Supplied through the generosity of the Ethicon Suture Laboratories, Inc., New Brunswick, N. J.

sels, there is a great hazard of catching a fine fragment of the opposite wall, destroying the patency of the anastomosis. The technique described eliminates this danger. The long end (A) of one suture, AB' (Fig. 1), was run as a simple continuous over-and-over stitch, uniting the vessels posteriorly; this suture was tied (AA') to the short end of the stitch at the opposite angle. The anterior row was constructed similarly, from B to B'. Visualization of the posterior wall often was facilitated by rotation of the vessels on their long axis, as demonstrated in Fig. 2.

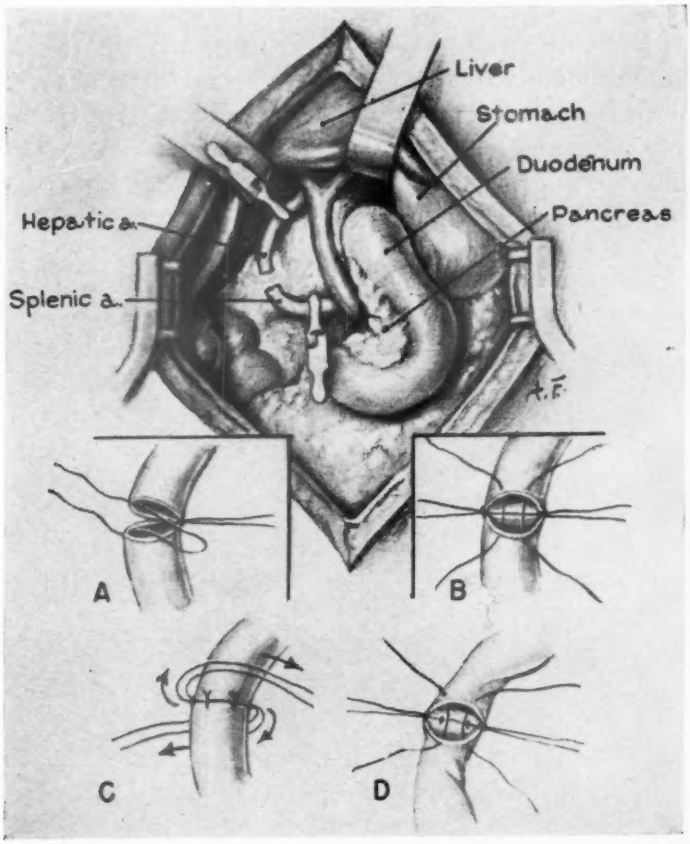


Fig. 2.—*Upper,* Splenic artery brought behind duodenum for splenohepatic anastomosis; *Lower,* anastomosis facilitated by rotation of vessels.

Although an everting type of suture might seem preferable in most vascular surgery, approximating intima to intima, the narrowing of the vessel lumen produced by such a method unfavorably influences its satisfactory use in arteries of this small caliber. The stitch includes all the layers of the vessel wall, each bite of the needle meticulously being placed less than 1 mm. from the cut end of the artery. Thus, a one-layer, very slightly inverting type of anastomosis is effected. The suture line has been loosely wrapped with compressed Gelfoam,* as an aid in securing hemostasis on release of the bulldog

*The Gelfoam and heparin sodium were made available through the courtesy of the Upjohn Company, Kalamazoo, Mich.

clamps; in most instances this has not been absolutely essential. The animals utilized for investigation of the superior mesenteric artery were heparinized after mobilization of the vessels, receiving 1 c.c. (1,000 U.S.P. units, 10 mg.) of heparin sodium solution† intravenously per ten pounds of body weight. Neutralization of the heparin with protamine was necessary in only a few operations, when oozing from the abdominal wound presented a problem.

A layer closure of the abdominal wall completed the procedure. All animals received an intravenous infusion of 1,000 c.c. of 5 per cent dextrose in physiologic saline solution during operation. Aureomycin, 500 mg., was administered through a Levin tube during operations involving the superior mesenteric artery. Penicillin, 300,000 U., was given intramuscularly daily for three days to all animals, except those in which the hepatic artery was under study. Antibiotics were withheld in this group, in an attempt to avoid masking or favorably influencing an unsatisfactory anastomosis. The animals were observed during survival periods ranging from 7 to 295 days before they were sacrificed for the final observations.

RESULTS

Replacement of Hepatic Artery.—In each of these operations, the main hepatic artery was mobilized in the posterior portion of the hepatoduodenal ligament, close to its origin from the celiac axis, and proximal to any major branches of the hepatic. An anastomosis was constructed between the distal end of the divided hepatic artery and the proximal stump of either the splenic or the right renal artery.

TABLE I. SPLENOHEPATIC ARTERIAL ANASTOMOSIS

DOG	SURVIVAL (DAYS)	STATUS OF ANASTOMOSIS	
		END-TO-SIDE	END-TO-END
S.H. 1	97	Patent	
S.H. 2	50	Occluded	
S.H. 3	65	Occluded	
S.H. 4	91	Patent	
S.H. 6	137		Occluded
S.H. 7	98		Occluded
S.H. 8	154		Occluded
S.H. 9	82		Occluded
S.H. 10	83		Patent
S.H. 12	77		Occluded
S.H. 14	295		Occluded
S.H. 18	187		Patent
S.H. 22	175		Occluded
S.H. 24	151		Patent
S.H. 25	146		Occluded

Splenohepatic arterial anastomosis: The spleen was mobilized and resected, with division of the splenic artery close to the hilus and preservation of a generous length of the vessel (Fig. 3). The splenic artery was passed behind the duodenum, to come into position near the hepatic artery, and the ends of the vessels were joined (Fig. 4). Twenty-one dogs were subjected to this procedure, of which eight animals died during the first postoperative week. The anastomoses were found to be patent in two of these; liver

necrosis and peritonitis were present in three of the six with occluded anastomoses. Death occurred in two additional dogs, on the eleventh and eighteenth days, respectively, and in each instance an occluded anastomosis and peritonitis were found.

The remaining eleven dogs were in healthy condition when sacrificed, at intervals from 77 to 295 days postoperatively. The anastomoses were patent in only three dogs, and they were thrombosed in the remainder. In an additional series of five dogs, an anastomosis was effected between the end of the splenic artery and the side of the intact hepatic artery. Patent anastomoses were found in two of the four dogs surviving into the period of observation. The livers of the surviving dogs with open anastomoses were not significantly different from those in the occluded group, in either series. The long-term results are summarized in Table I.

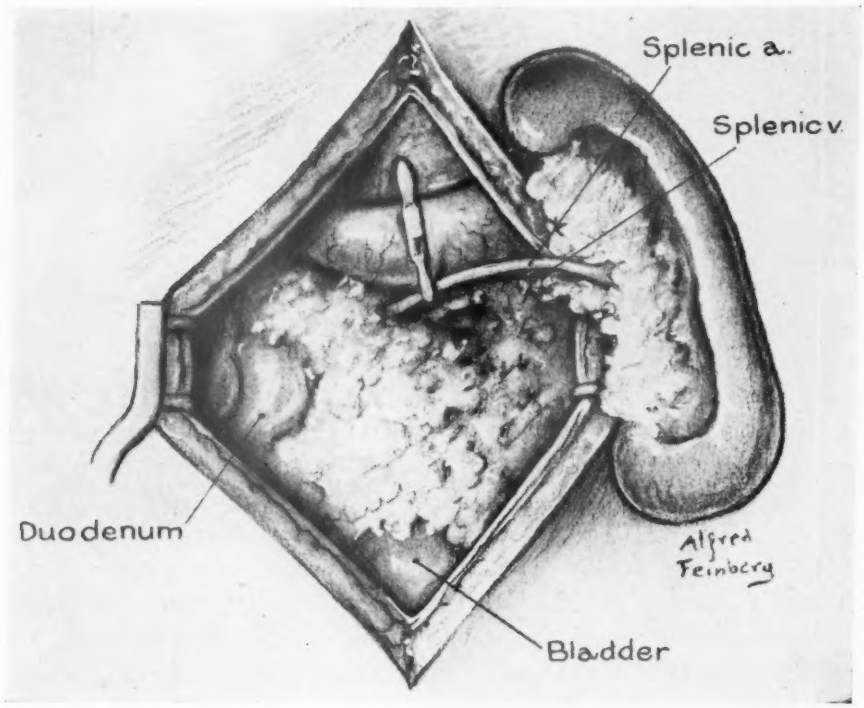


Fig. 3.—Spleen mobilized, with long segment of splenic artery available for anastomosis to hepatic, mesenteric, or renal arteries.

Chronologically, these were the earliest experiments in this program. The generally unsatisfactory results may be attributed in large part to inexperience, as the technical steps for the facile construction of such anastomoses were still being evolved. In addition, mobilization of the splenic artery and splenectomy are not practical from the right side of the abdomen, where the operator would be working if he were in the vicinity of the hepatic artery. The retroduodenal passage of the vessel poses another problem. All of these difficulties were obviated subsequently by use of the right renal artery. The splenic artery taken near its origin might also be adequate.

Renal-hepatic arterial anastomosis: The right kidney was mobilized and resected, with preservation of most of the length of the main renal artery. The similarity in size of the renal and hepatic arteries, and the ease with which these vessels could be approximated, made this a most favorable situation (Fig. 5). The operation was performed on five dogs, with death of one animal due to aspiration under anesthesia. Three of the survivors were subsequently subjected to splenomesenteric arterial anastomosis, and these results will be analyzed in Table II. There was one occluded renal-hepatic arterial anastomosis.

TABLE II. RENAL-HEPATIC ARTERIAL ANASTOMOSIS

DOG	SURVIVAL (DAYS)	STATUS OF ANASTOMOSIS	
		RENAL-HEPATIC	SPLENOMESENTERIC
R.H. 1	30	Patent	
R.H. 3	66	Patent	Occluded P.O. 38
R.H. 4	38	Patent	Patent P.O. 15
R.H. 5	19	Occluded	Patent P.O. 7

Replacement of the Superior Mesenteric Artery.—In each of these experiments the superior mesenteric artery was mobilized and ligated as it arose from the aorta. The proximal 1 to 2 cm. of this vessel are free of any branches, and it is in this area that the vessel was divided. Heparinization was accomplished initially by injection into the mesenteric artery, but this had no real advantage over the intravenous route employed in the later experiments. As soon as the artery was ligated, the color of the small bowel changed to a dull white and pulsations disappeared from the mesentery. The usual period of arterial occlusion was about twenty-five minutes. Release of the occluding clamps, after completion of the anastomosis, was followed by a return to normal color in the bowel and often by visible and palpable pulsations in the mesentery. This return was manifested in some areas of the bowel more promptly than in other segments. In contrast to the similarity in size of the other vessels studied, the superior mesenteric artery was consistently, and often considerably, larger in diameter than the splenic or renal arteries. The difficulties created by this disparity in size were often met by one or another of the technical variations illustrated in Fig. 6. A palpable thrill was usually detected distal to anastomoses of vessels with markedly different diameters.

Splenomesenteric arterial anastomosis: This was performed in two different ways. A long segment of splenic artery was prepared in the earlier experiments, following splenectomy, and this was brought down to the mesenteric artery. Utilization of this procedure on seven dogs resulted in three survivals with patent anastomoses. Occlusion of the anastomosis uniformly resulted in gangrene of the bowel and death of the animal. Subsequently it became obvious that the splenic artery at its origin from the celiac axis possessed many advantages. The two vessels are situated in close proximity, the

Fig. 4.—Diagrams and specimens of splenohepatic arterial anastomoses, end-to-end, 151 days, and end-to-side 97 days postoperatively.

diameter of the splenic artery is larger at its source than at the periphery, the wall of the splenic artery is thicker in this location, and the spleen need not be removed. This procedure was performed on eleven dogs, with seven survivals, including three animals previously subjected to right renal-hepatic

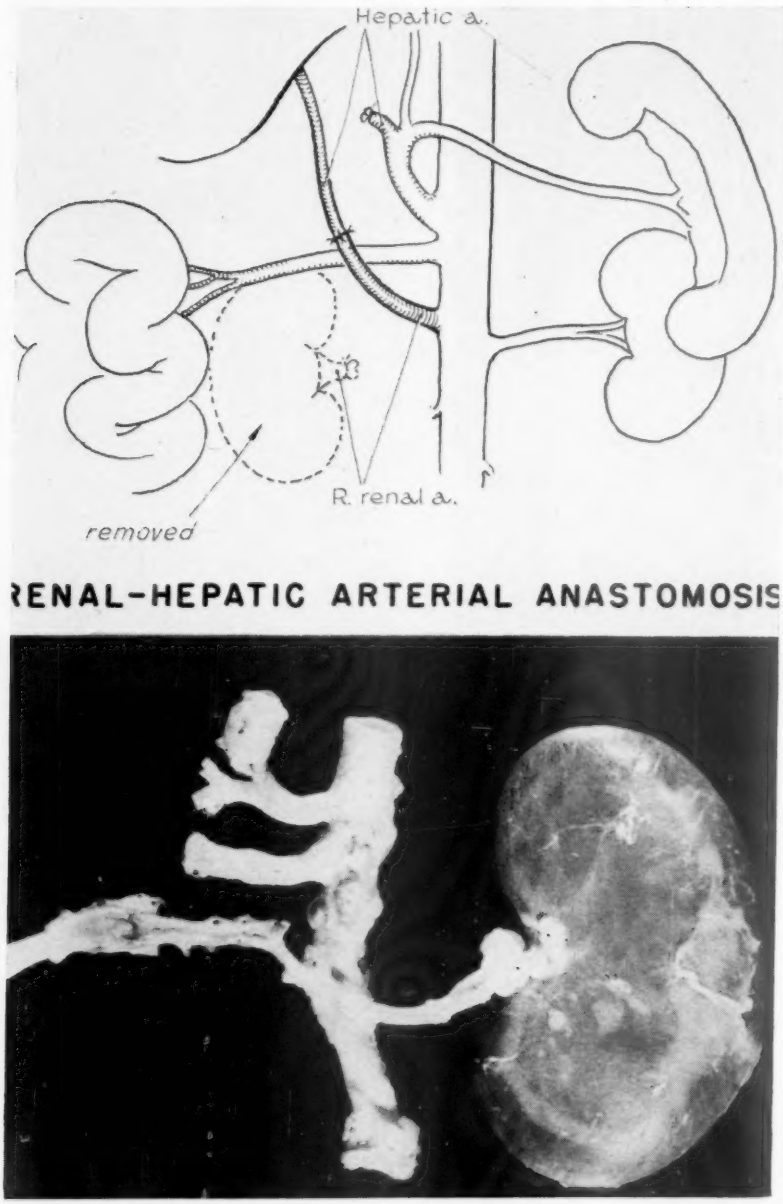


Fig. 5.—Diagram and specimen of renal-hepatic arterial anastomosis, thirty days postoperatively.

arterial anastomoses. One of the latter survivors, R. H. 3, had viable bowel with an occluded anastomosis, the only such instance encountered in this series. Another dog (S.M. 23) had apparently been injured some time before. At operation the spleen was found to be divided into two unequal portions,

and the omentum was studded with implants of splenic pulp. This example of splenosis will be studied further. The operative procedures are illustrated in Figs. 7 and 8, and summarized in Table III.

TABLE III. SPLENOMESENTERIC ARTERIAL ANASTOMOSIS

DOG	DIAMETER OF ARTERY (MM.)		DURATION OF ARTERIAL OCCLUSION (MINUTES)	SURVIVAL (DAYS)	STATUS OF ANASTOMOSIS
	SPLENIC	MESENTERIC			
S.M. 7*	1.5	4	33	1	Occluded
S.M. 8*	5	7	51	82	Patent
S.M. 9*	3	5	27	1	Occluded
S.M. 10*	2.5	5	44	1	Occluded
S.M. 11*	3	7	69	1	Occluded
S.M. 12*	3	6	51	6	Patent
S.M. 13*	2	5	42	11	Patent
S.M. 14†	4	5.5	28	14	Patent
S.M. 15†	2.5	4	16	27	Patent
S.M. 16†	3	5	15	5	Occluded
S.M. 17†	5	7	15	16	Patent
S.M. 20‡	3.5	6	22	2	Occluded
S.M. 21§	3.5	7	63	2	Occluded
S.M. 22†	3	5.5	23	2	Occluded
S.M. 23†	3	5	19	25	Patent
R.H. 3†	3.5	6	16	38	Occluded
R.H. 4†	3	5	19	15	Patent
R.H. 5†	3	6	30	7	Patent

*Long splenic artery, interrupted sutures.
†Splenic artery at origin, continuous sutures.
‡Splenic artery at origin, continuous sutures. Splenic artery twisted (poor technique).
§Splenic artery at origin, continuous sutures. Splenic artery lacerated (poor technique).

Renal-mesenteric arterial anastomosis: The left kidney was sacrificed, preserving the left renal artery. The left renal and superior mesenteric arteries could be brought together in satisfactory fashion (Fig. 9). Since this procedure had already been performed by Kremens,[3] no attempt was made to do more than verify his observation, and therefore we operated on only three dogs. Of these, one had a patent anastomosis at autopsy, thrombosis had occurred in the second, and the third succumbed eight days postoperatively as the result of disruption of the suture line, the only such complication in the

TABLE IV. LEFT SPLENORENAL ARTERIAL ANASTOMOSIS

DOG	DATE OF ANASTOMOSIS	DATE OF RIGHT NEPHRECTOMY	SURVIVAL (DAYS)	STATUS OF ANASTOMOSIS
S.R. 1	Oct. 7, 1952	Oct. 24, 1952	148	Patent
S.R. 2	Oct. 8, 1952	—	4	Patent
S.R. 3	Oct. 10, 1952	Nov. 4, 1952	125	Patent
S.R. 4	Oct. 24, 1952	Nov. 4, 1952	76	Patent
S.R. 5	Oct. 28, 1952	—	14	Occluded
S.R. 6	Oct. 31, 1952	Nov. 13, 1952	75	Patent

entire series. There was less disparity between the diameters of the renal and mesenteric arteries than was the case when the splenomesenteric shunts were constructed.

Replacement of the Renal Artery.—Splenectomy and left splenorenal arterial anastomosis, followed by right nephrectomy several days later, con-

stituted the plan for this experiment (Fig. 10). The combined procedure was completed satisfactorily in four of the six dogs selected for this purpose, as shown in Table IV. One dog (S.R. 2) died on the fourth postoperative day of an aspiration pneumonia. An infarcted left kidney was found in another animal (S.R. 5) at the time of the second laparotomy. Renal function was adequately maintained in the survivor group by the splenic arterial inflow to the solitary left kidney, which in every instance at autopsy was normal in color and considerably larger than at the time of the original operation.

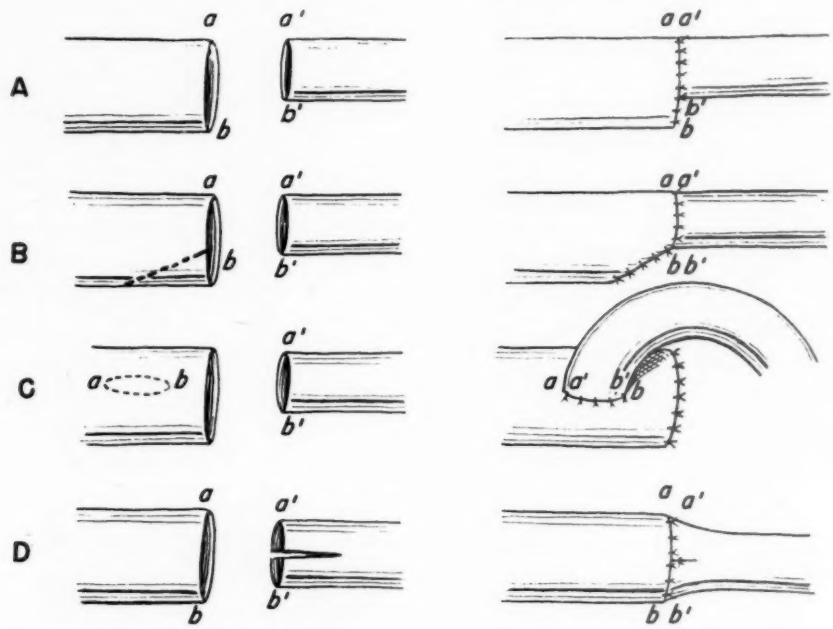


Fig. 6.—Alternate maneuvers for the anastomosis of vessels with wide discrepancy in size.

DISCUSSION

These investigations would suggest that it makes very little difference whether silk or catgut is used for vascular surgery of this type. It is essential that the suture material be as fine as possible, that it be well lubricated, and that it be passed in such a way as to inflict a minimum of trauma to the vessel. When these conditions are observed, the incidence of thrombosis and extent of traumatic or foreign body reaction is approximately the same. Everting and interrupted sutures were less successful in these small vessels than a simple over-and-over, continuous stitch, interrupted only at the lateral angles.* The 00000 mild chromic catgut employed for many of these operations still presents two minor variables. The strands are not absolutely uniform in strength, so that occasionally one will break more easily than the others; this has been greatly improved in the past few years. And the time of disappearance of the catgut is highly unpredictable at present. In the surgery of blood vessels, no instances have been encountered when the cat-

*Dr. Emile Holman once remarked, during a visit to our laboratory, that Halsted might never have turned to silk if such fine catgut had been available.

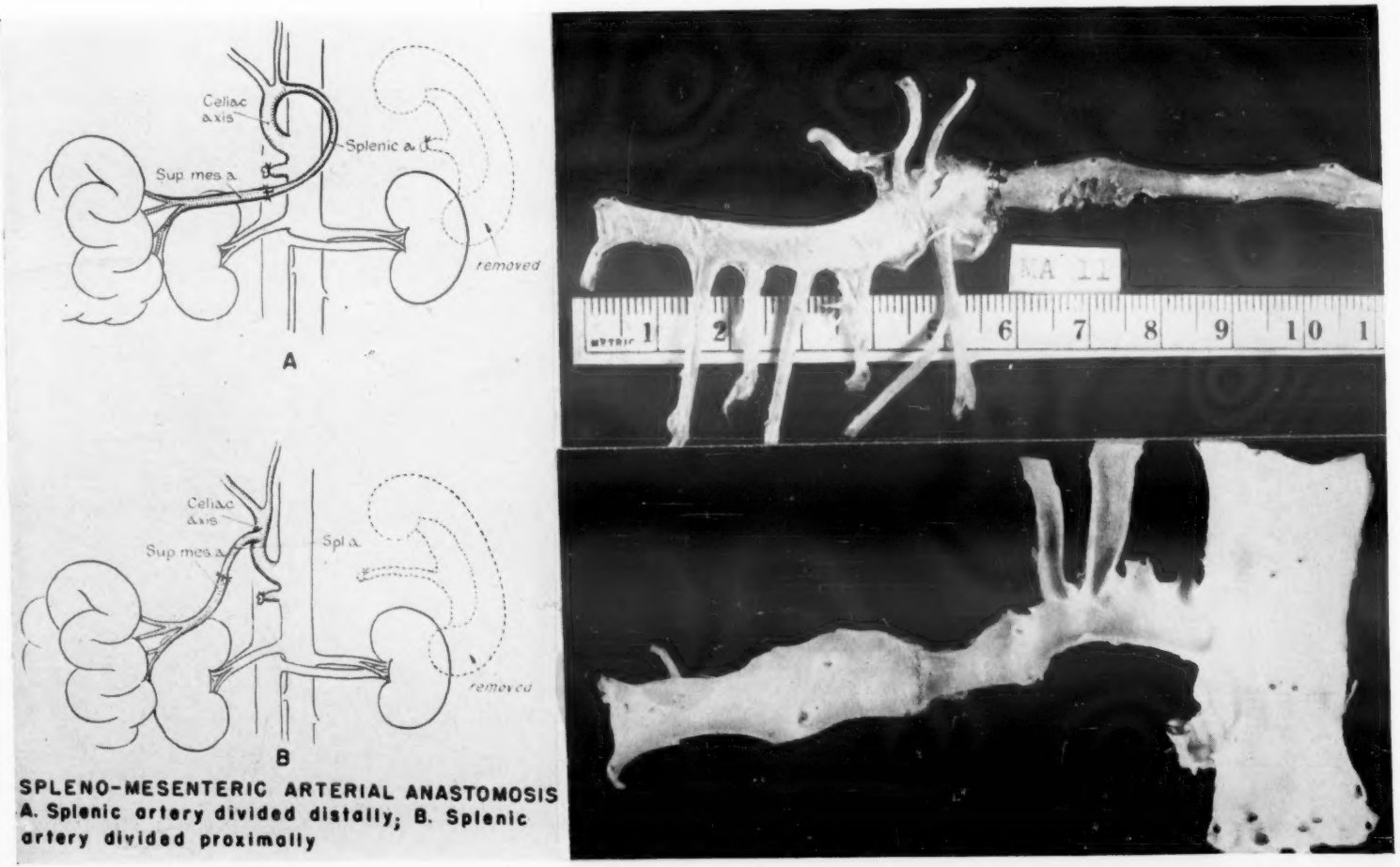
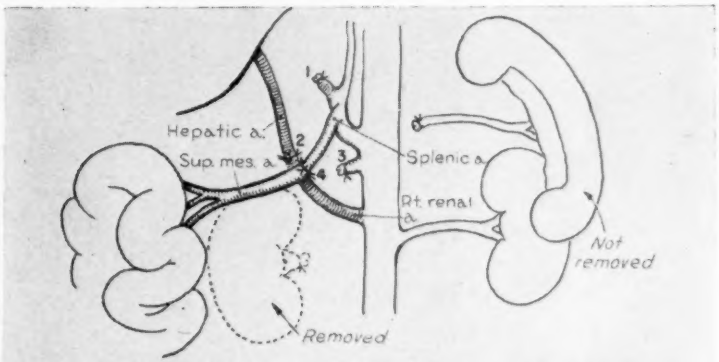


Fig. 7.—Diagrams and specimens of splenomesenteric arterial anastomoses, long splenic, eleven days, and short splenic, twenty-five days postoperatively.

gut was absorbed so quickly as to jeopardize the strength or integrity of the anastomosis. On the other hand, in some dogs sacrificed as long as six months postoperatively the individual strands of catgut could still be clearly identified.

The attempt was made to define the conditions of most of these experiments in such a way that they would be crucial, in the sense that an unsatisfactory anastomosis would be incompatible with survival of the animal. Re-



RENAL-HEPATIC AND SPLENO-MESENTERIC ARTERIAL ANASTOMOSES

1. Hepatic artery ligated proximally.
2. Anastomosis of right renal artery to distal hepatic artery.
3. Superior mesenteric artery ligated proximally.
4. Anastomosis of splenic artery to distal superior mesenteric artery.

Fig. 8.—Diagram and specimen of combined renal-hepatic (thirty-eight days) and spleno-mesenteric (fifteen days) arterial anastomoses postoperatively.

placement of the arterial blood supply to a solitary kidney by the splenic artery is the only situation in which this criterion was absolute. The one dog in the splenorenal series with an obstructed anastomosis and an infarcted left kidney had not yet undergone right nephrectomy. The anastomoses were patent in all the others, with a compensatory enlargement of the single kidney. Right nephrectomy in each instance was performed as a second stage procedure, rather than at the time of construction of the left splenorenal arterial anastomosis. The combined procedure should entail little additional difficulty.

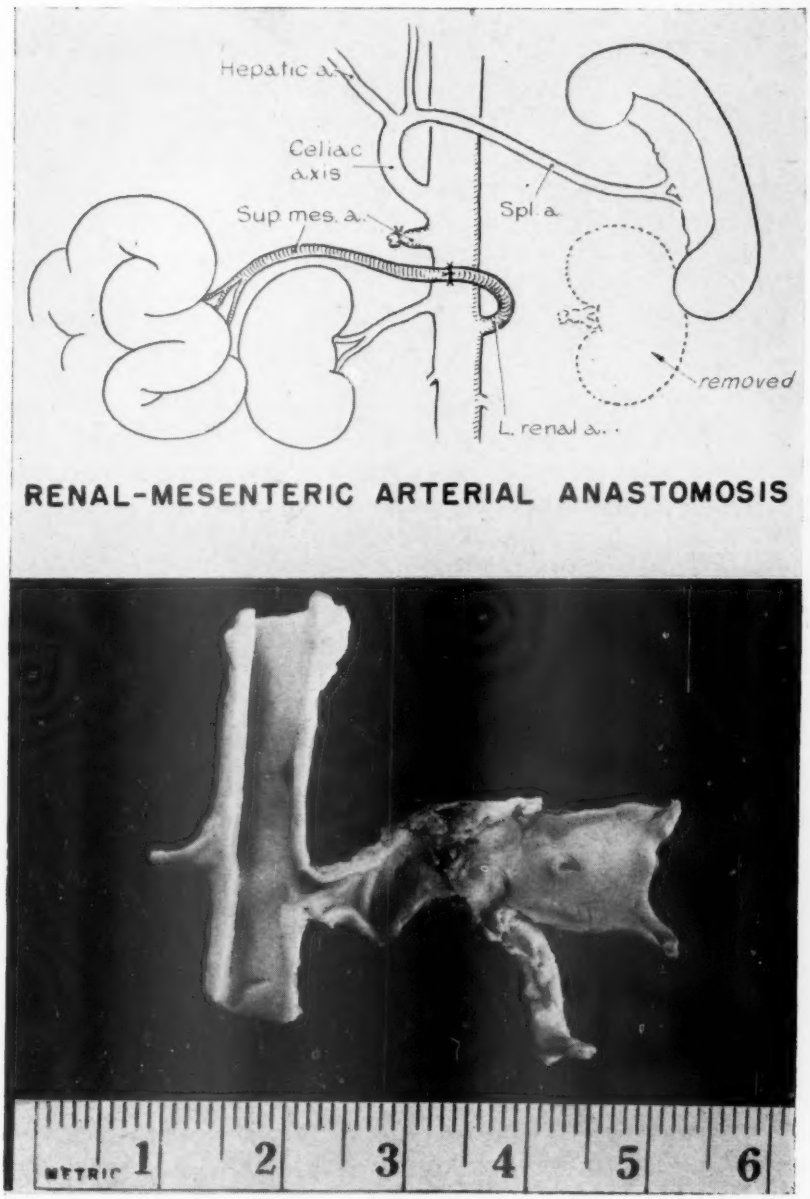


Fig. 9.—Diagram and specimen of renal-mesenteric arterial anastomosis, eighteen days postoperatively.

It would be anticipated that failure to reconstruct adequately the divided superior mesenteric artery would inevitably result in death. While this is usually true, in one instance sacrifice of an apparently healthy dog thirty-eight days after construction of a splenomesenteric arterial shunt unexpectedly disclosed a thrombosed arterial anastomosis. The clinical course of the animal and normal appearance of the small bowel at autopsy led the prosecutor to

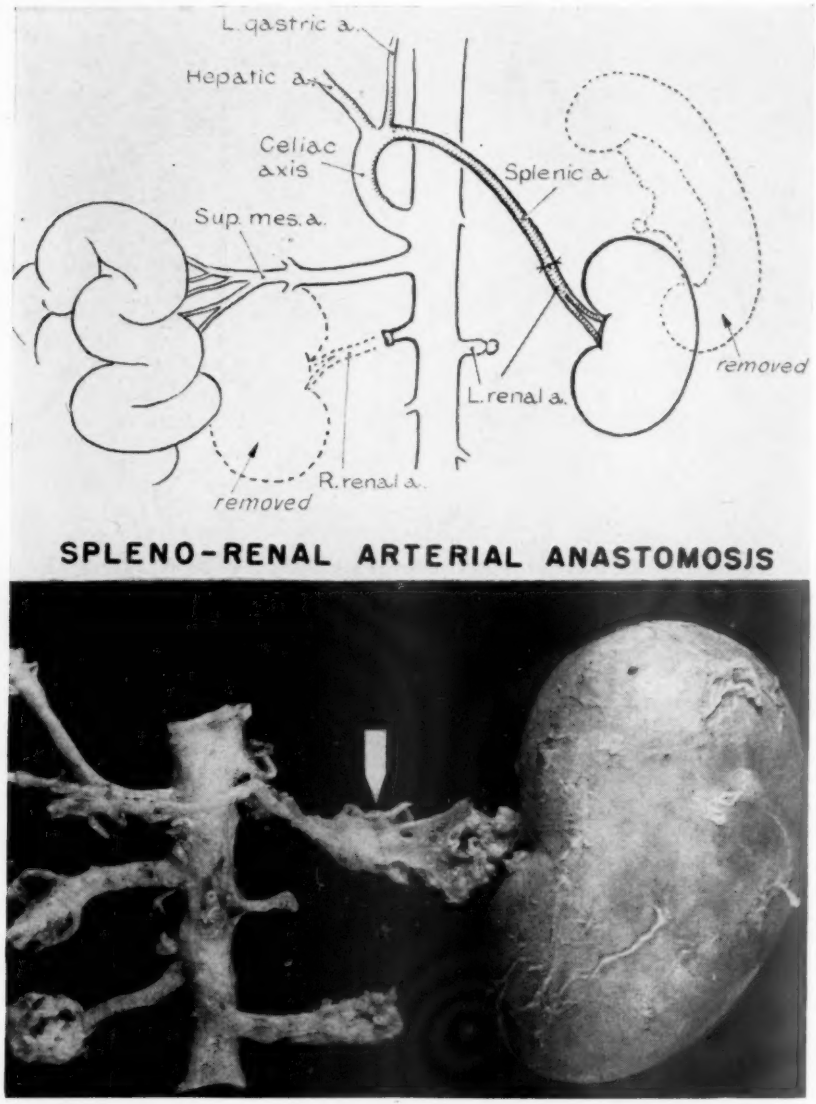


Fig. 10.—Diagram and specimen of splenorenal arterial anastomosis, seventy-five days postoperatively.

anticipate a patent vessel, so that it was not possible subsequently to reconstruct the collateral pathways by which arterial blood had reached the small bowel. These dogs were heparinized during the acute period of arterial occlusion, to minimize thrombosis of the mesenteric veins, as suggested by Nelson

and Kremens.[1] The introduction of Aureomycin into the gastrointestinal tract during the period of arterial deprivation, to inhibit the deleterious influence of intestinal bacteria, has been described by Rabinovici and Fine.[2]

Successful replacement of the superior mesenteric artery by the left renal artery has been accomplished in the dog by Kremens.[3] In the present series the renal artery was less satisfactory than the splenic artery for this purpose. The celiac axis has been demonstrated to be capable of delivering enough arterial blood to maintain the viability of the gastrointestinal tract from the lower esophagus to the midtransverse colon, including the liver, pancreas, and spleen, in apparently healthy dogs. In other dogs the hepatic component of this demand was adequately furnished by the right renal artery.

Attempts to reconstruct the superior mesenteric artery in man have not been reported. Embolectomy has been described by Klass,[4] with viable bowel described at autopsy following death of the patient due to cardiac failure. Either arterial replacement or embolectomy would seem preferable when possible to massive resection of the bowel, with which a successful outcome has so infrequently been achieved.[5] Winfield and Mersheimer[6] have summarized 212 instances of successful resections after mesenteric vascular occlusions (either arterial or venous), to which they have added five. Survival following expectant treatment has been extremely rare.

Reconstruction of both the superior mesenteric artery and vein at one operation was not successfully accomplished in this experimental series. Various combinations of procedures were tried, including both the renal and splenic arteries and veins, but all were unsatisfactory. Similar results have been referred to by Kremens,[3] who also felt that the problem was more complex than just the construction of two anastomoses.

Reconstruction of the superior mesenteric vein in the human being has been reported by Ripstein and Ostrow[7] and by Moore and co-workers.[8] McDermott[9] has described a patient in whom the superior mesenteric vein was anastomosed to the inferior vena cava. On the other hand, experiences involving ligation of the superior mesenteric vein in the laboratory and in human beings have recently been summarized,[10, 11] and this has been accomplished successfully in one case at the Montefiore Hospital.[12] Adequate criteria are currently lacking for the selection of the cases in which the superior mesenteric vein may be sacrificed with impunity.

When this program was initiated, it was erroneously believed that survival of a dog following division of the hepatic artery and its reconstruction with the splenic or right hepatic artery was an indication of patency of the anastomosis. Penicillin was not used, since Markowitz[13] had demonstrated the protective action of this agent. The hepatic artery had consistently been ligated close to its origin from the celiac axis, and several recent studies have demonstrated that this often permits an adequate collateral arterial circulation to the liver.[14-18] This has been corroborated by finding normal livers in healthy animals sacrificed early in this series, with thrombosed splenohepatic and renal-hepatic arterial anastomoses. The wide variation in an-

atomic potential for the maintenance of hepatic survival must explain the fact that ligation of the normal hepatic artery in human beings, whether deliberate or accidental, may be followed by death[19-21] or by recovery.[22-25]

The occurrence of aneurysms of the intra-abdominal arteries presents a considerable challenge to the surgeon. Involvement of nonessential vessels, such as the left gastric and splenic arteries, lends itself nicely to surgical excision, whereas fatal hemorrhage may result if perforation occurs.[26, 27] Rupture of an aneurysm of the hepatic artery is similarly to be feared.[28] Ligation of the hepatic artery for aneurysm has been performed successfully in only three instances, according to Grant and associates[29] with death from liver necrosis or recurrent hemorrhage the more frequent result of this procedure. Dwight and Ratcliffe[30] summarized ninety-one previously reported cases of aneurysm of the hepatic artery, with survival following treatment by wiring in one patient. Both of these reports speculate on the theoretical preferability of excision of the aneurysm, with restoration of the continuity of the vessel, either by end-to-end suture or by a graft.

Cadaver dissections on autopsy material at this hospital have clearly demonstrated the anatomic feasibility of utilizing the right renal artery to replace the hepatic artery or the splenic artery to replace either the superior mesenteric or left renal arteries. The advantages of using, as an arterial shunt, a segment of fresh, autogenous artery, already attached at one end, are obvious, and have previously been documented in this laboratory.[31] Such clinical use of the splenic artery, to by-pass a low coarctation of the aorta, was postulated by Blalock[32] and carried out by Glenn and co-workers.[33] Freeman and Leeds[34] have swung the splenic artery around aneurysms of the abdominal aorta.

Either the renal or the splenic artery could be used for the arterialization of the blood supply to the liver, now accomplished by other techniques in several experimental programs.[35-37] One approach already described for increasing the supply of oxygenated blood to the liver has been by splenectomy with anastomosis of the splenic artery and splenic vein.[38] In one group of the present experiments, it has been shown that it is possible to anastomose the free end of an auxiliary artery, such as the splenic or renal, to the side of the intact hepatic artery. Whether or not this results in augmenting the flow of blood through the hepatic artery awaits further study. The investigations of Kantrowitz concerning the potential increase in arterial flow to be gained by an ancillary vessel of such a length as to be out of phase with systole of the coronary artery suggest such an application.[39]

One consideration that must be taken into account when speculating on the interpretation of these experimental data in terms of human surgical problems is the time factor. The elective replacement of aneurysms or of vessels involved by neoplasms would permit preparation of the graft prior to approaching the lesion, ensuing a minimum period of deprivation of arterial blood for the essential organ. Salvage of a situation in which an essential artery has been lacerated or compromised accidentally during the course of an operation would entail a longer, but not unreasonable, period of such depriva-

tion. Unfortunately, the time lag between embolic or thrombotic occlusion of a mesenteric or renal artery and laparotomy is such that gangrene has usually already developed, precluding vascular surgery. The basic problem is similar to that posed by thrombosis of the cervical portion of the internal carotid artery, where speed of diagnosis and prompt surgery are essential.[40] A high index of suspicion plus a recognition of the possible role of blood vessel surgery may result in an improved technique for the management of these patients.

SUMMARY

1. In a series of dogs, it has been shown that the hepatic, superior mesenteric, or renal arteries may be sacrificed and satisfactorily replaced by other intra-abdominal arteries.

2. Clinical application of these techniques is suggested in the management of compromise of these essential vessels by accidental injury, aneurysm, neoplasm, or thromboembolic occlusion.

Acknowledgment.—We wish to express our appreciation to Dr. Harry M. Zimmerman, chief of the Laboratory Division, for making available the facilities of the autopsy room, and to Mr. Ruthven Ferreira for invaluable technical assistance with every phase of the investigation.

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THE USE OF NYLON NET FOR THE EXTERNAL SUPPORT OF BLOOD VESSEL GRAFTS AND ANEURYSMS

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LONG-TERM follow-up observations of blood vessel grafts in animals have shown a significant incidence of dilatation, thinning, and even aneurysm formation.[1-15] These changes have been observed both in homologous artery and autologous vein grafts. Other tissues, such as fascia lata and pericardium, have shown an even greater tendency to undergo these changes. Although synthetic materials used as prostheses have shown encouraging results,[16, 17] most vascular surgeons rely on the use of blood vessels for replacement. If this type of replacement is to continue, it is evident that measures must be taken to insure its anatomic and functional integrity over a long period of time. It is the purpose of this report to present a technique which appears to meet such a need by means of external support.

MATERIALS AND METHOD

An open-mesh, tulle-woven net of a nylon resin polymer* was selected for this study (Fig. 1, *A*). Its most outstanding qualities for this use were tensile strength, elasticity of the filament, and the fact that the fibers are knotted where they cross. In addition, this material has been well tolerated in animal tissues for long periods of time.

Before undertaking any operative procedures, tubes of this material were fashioned of varying lengths and diameters. Carefully measured pieces of the net were folded longitudinally, and the free edges were sewn with nylon thread (Fig. 1, *B*). The greatest elasticity was achieved by aligning the fibers at a forty-five degree angle to the long axis. The diameter of the tubes varied from 6 to 15 mm., and the length from 6 to 10 cm. In order to facilitate use at operation, the tubes were telescoped in accordion fashion over matching glass tubes, and were held in this state by encircling silk sutures (Fig. 1, *C*). Since a plasticizer is used with nylon of textile grade, pretreatment by immersion in a detergent solution, followed by boiling in water, is necessary. The tubes could then be stored for instant use. This material can safely be sterilized repeatedly by boiling, autoclaving, or dry heat without alteration of its characteristics.

Forty-two adult mongrel dogs weighing from 7.5 to 18 kilograms were used. Intravenous pentobarbital sodium (30 mg. per kilogram) was employed for anesthesia. These experiments were divided into three groups.

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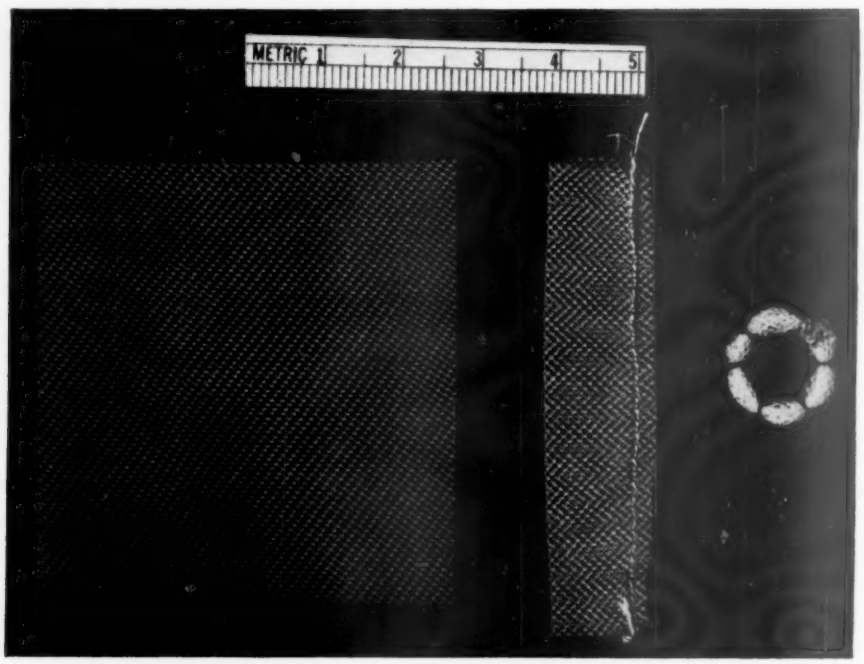
*Supplied by Ethicon Suture Laboratories, New Brunswick, N. J.

1. *External jugular venous autografts implanted into the abdominal aorta (twelve dogs).*—An incision was made in the neck over the vein, and a segment free of valves was resected. The length varied from 2.8 to 4.8 cm. After irrigation with heparin-saline solution, the grafts were placed in cool saline solution. The abdomen was then opened through the midline, and the aorta exposed. This vessel was mobilized in its bed by division of lumbar branches, and a segment below the renal arteries measuring 1.5 to 2.5 cm., depending on the length of the graft to be implanted, was resected. The venous grafts were then sutured into place, employing a continuous suture of 00000 braided arterial silk.*



A. *B.* *C.*

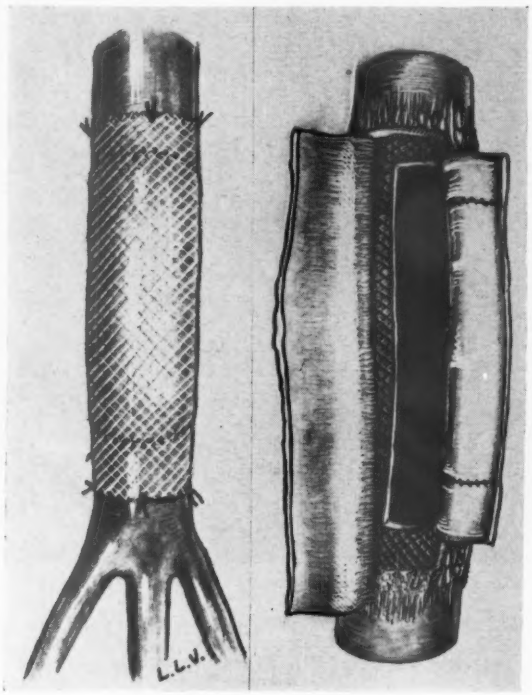
Fig. 1.—*A*, Tulle-woven net of nylon fibers. *B*, Nylon net folded longitudinally and its free edge sewn to form a tube. *C*, Nylon net tube telescoped upon itself and secured with encircling silk ligatures to facilitate its application over the graft.

A previously prepared nylon tube of proper length and diameter was slipped over the graft before beginning the final anastomoses. The transfixion sutures of the tube were cut, and the tube was drawn out over the graft. In all instances, the nylon net extended beyond the graft for 1.0 to 1.5 cm. (Fig. 2, *A*). The occluding clamps were brought closer together so that the net could be sutured to the host aorta with the suture lines relaxed. When blood flow was restored through the graft, there was minimal tension on the anastomoses. In all these dogs, the diameter of the supported graft equaled that of the host aorta, or was smaller by 1.0 to 1.5 mm. Careful measurements were made with calipers. Eight grafts were reinforced by nylon net, and four were implanted without support to serve as controls.

2. *Pericardial tubes implanted into the thoracic aorta (nine dogs).*—After performing a left thoracotomy, a sheet of autologous pericardium, 4 by 5 cm.,

*Supplied by J. A. Deknatel and Son, Queens Village, N. Y.

was excised. Tubes were constructed so as to conform to the diameter of the host aorta after the method of Sako.[6] The descending thoracic aorta was mobilized by division of the intercostal arteries, and a segment measuring from 2.0 to 2.5 cm. was excised. The pericardial graft was slipped over a 6.0 by 0.6 cm. polyethylene tube, which in turn was ligated into the aorta to allow blood flow during implantation. Before completion of the final anastomosis, the aorta was reoccluded briefly, during which time the tube was removed and the suture line completed. In five animals a telescoped nylon tube was slipped over the pericardial graft, before the polyethylene tube was ligated in place. After implantation was completed, the nylon tube was treated as in the first group of animals. In four, no external support was used. The length of the pericardial graft after implantation varied from 3.0 to 4.3 cm., and the outside diameter matched that of the host aorta.



A. *B.*

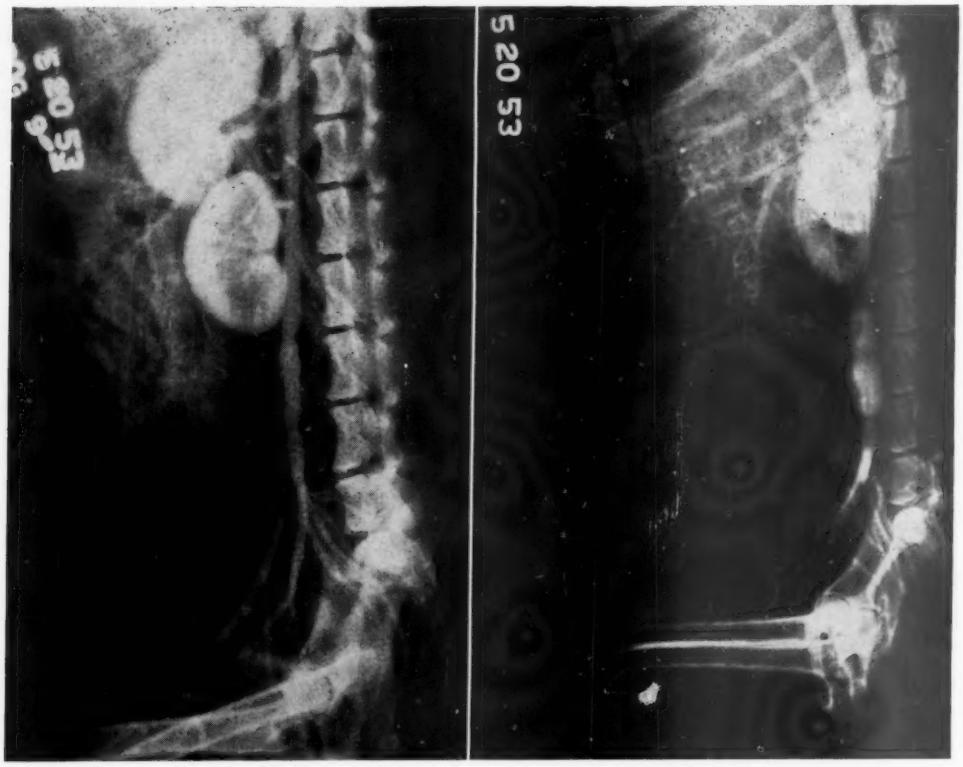
Fig. 2.—*A*, Drawing of a vein graft supported by a nylon net tube implanted into the abdominal aorta. Note that the net extends beyond each anastomosis and is sutured to the host vessel.

B, An artist's drawing showing the relationship of the nylon net to the graft and the investing fibrous tissue.

3. *Vena caval autografts implanted into the abdominal aorta (twenty-one dogs).*—Segments of inferior vena cava measuring from 3.5 to 5.0 cm. were implanted into the abdominal aorta of the same dog by the technique described in Group 1. All these grafts had a diameter 1 to 4 mm. greater than that of the host aorta. Nylon net was applied to all of these, and since its diameter was the same as that of the host aorta, the disproportion was greatly reduced or eliminated when the net was extended over the graft.

RESULTS

Upon resumption of blood flow, there was an immediate distention of the grafts to the limits imposed by the investing nylon net. The graft and net pulsed synchronously with the adjacent normal aorta. There was a transitory oozing of blood from the anastomoses, which was less noticeable when the nylon net overlay the suture line. The contour of the aorta, anastomoses, and graft was uniform, and there was no evidence of turbulence.



A. *B.*

Fig. 3.—*A*, External jugular vein autograft supported by nylon net 301 days after implantation into the abdominal aorta of a dog.

B, An unsupported external jugular vein graft implanted for 237 days. Note the dilatation and the abrupt change in contour at the suture lines.

The grafts were studied at intervals by aortography, and ultimately by exploration and sacrifice. In this initial report, most of the observations have been derived from aortography, since the surviving animals are being studied for an extended period of time.

In Group 1, the status of the grafts of external jugular vein was studied over a period of from 36 to 305 days (Table I). In the eight dogs with external support by nylon net, there was no significant dilatation nor irregularity of the grafts (Fig. 3, *A*). On the contrary, in the four dogs in which no external support was present there was moderate to marked irregularity in all, and dilatation of from 25 to 40 per cent had occurred (Fig. 3, *B*). In two dogs,

sacrificed at thirty-six and forty-three days, there had been little or no thickening of the graft, whereas a 2 mm. layer of fibrous tissue had formed external to and through the interstices of the nylon net (Figs. 2, *B*, and 4).

TABLE I. EXTERNAL JUGULAR AUTOGRAFTS IMPLANTED IN THE ABDOMINAL AORTA OF DOGS

DOG	NYLON NET USED	PERIOD OF OBSERVATION (DAYS)	LENGTH (CM.)	INITIAL DISPROPORTION	PATENCY	DILATATION	CONTOUR	STATUS
901	Yes	36	4.8	None	Complete	None	Regular	Dead
899	Yes	43	3.5	None	Complete	None	Regular	Dead
900	Yes	301	3.8	None	Complete	None	Regular	Alive
898	Yes	293	3.0	None	Complete	None	Regular	Alive
896	Yes	291	3.3	None	Complete	None	Regular	Alive
907	Yes	277	3.4	None	Complete	None	Regular	Alive
908	Yes	276	2.8	None	Complete	None	Regular	Alive
944	Yes	223	3.5	None	Complete	None	Regular	Alive
904	No	305	4.3	None	Complete	35 per cent	Irregular	Alive
894	No	298	3.8	Slightly smaller than aorta	Complete	25 per cent	Irregular	Alive
934	No	237	3.7	Slightly smaller than aorta	Complete	40 per cent	Irregular	Alive
938	No	236	4.0	None	Complete	25 per cent	Irregular	Alive

In Group 2, the pericardial grafts were observed over a period of from 2 to 229 days (Table II). In the five dogs with external support, there was no significant dilatation or irregularity of the grafts (Fig. 5, *A*). Since one dog was killed at two days, no conclusions can be derived from this animal. Of the four dogs without nylon net, three were studied for from 40 to 229 days, and two showed definite dilatation and irregularity (Fig. 5, *B*). One dog died at three days from hemorrhage; a dehiscence had occurred in the vertical suture line of the graft. It is possible that this might not have occurred had the graft

TABLE II. PERICARDIAL AUTOGRAFTS TO THORACIC AORTA OF DOGS

DOG	NYLON NET USED	PERIOD OF OBSERVATION (DAYS)	LENGTH (CM.)	INITIAL DISPROPORTION	PATENCY	DILATATION	CONTOUR	STATUS
919	Yes	2	3	None	Complete	None	Regular	Dead
941	Yes	25	4.2	None	Complete	None	Regular	Dead
954	Yes	20	3.9	None	Complete	None	Regular	Dead
951	Yes	221	4.1	None	Complete	None	Regular	Alive
957	Yes	215	4.3	None	Complete	None	Regular	Alive
940	No	3	4.2	None	Complete	None	Regular	Died (hemorrhage)
955	No	40	3.8	None	Small mural thrombus	Dilated	Irregular	Dead
945	No	229	3.9	None	Complete	None	Irregular	Alive
952	No	206	3.9	None	Complete	Dilated	Irregular	Dead

been supported by the nylon net. Three grafts examined at autopsy between twenty and forty days revealed the same type of fibroblastic response as in Group 1. However, there was also noted a tendency for subintimal deposition of cholesterol as reported by Sako.[6]

In Group 3, the caval grafts were observed over a period from 1 to 268 days. In none of these dogs was there noted any dilatation. In one, the internal contour was slightly altered due to a thrombus, and in another, there was complete occlusion by thrombosis at nine days. In the latter, there was a marked constriction of the proximal suture line. Of nine dogs studied at autopsy, only two were killed beyond ten days after operation. In these killed, at thirty-three and eighty-two days, there was the usual fibrotic thickening occurring external to the graft.

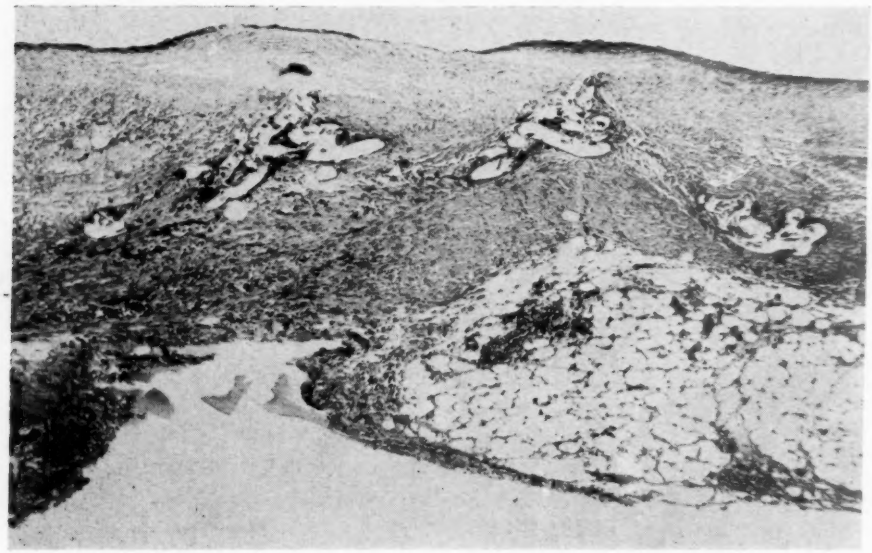


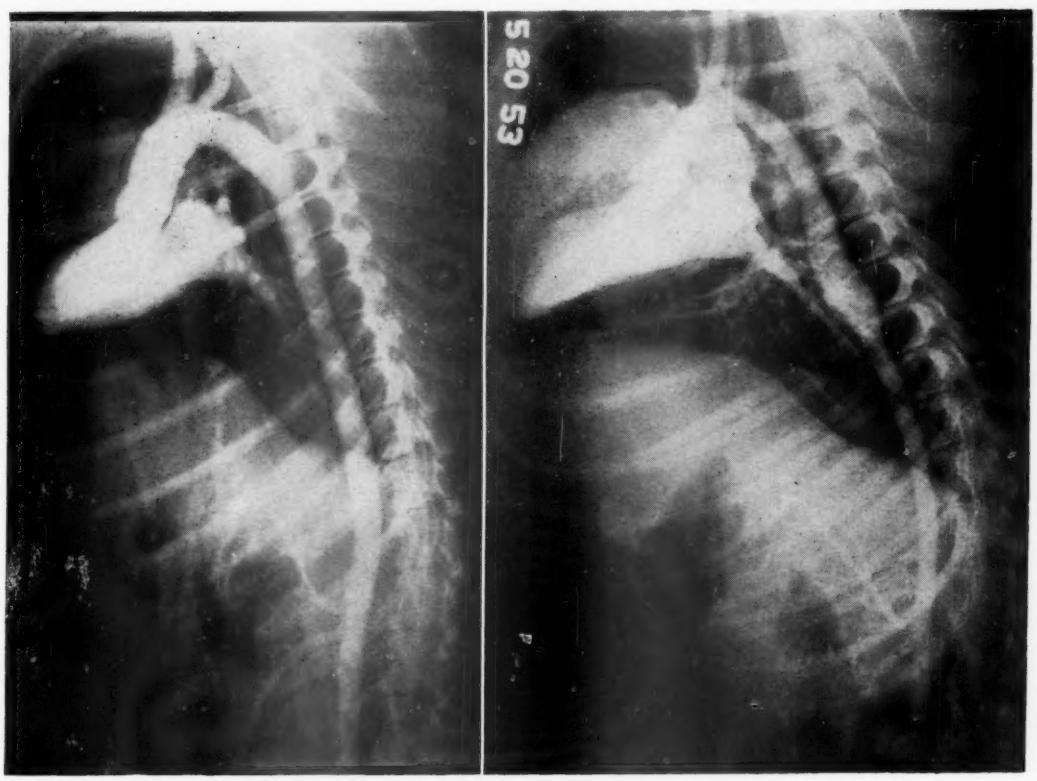
Fig. 4.—Photomicrograph of a vein graft supported by nylon net, 43 days after implantation. Note the position of the nylon fibers between the graft above and the investing fibrous tissue below. (Trichrome stain ×30, reduced one-third.)

In summary, it has been demonstrated that no significant dilatation has occurred in any of the thirty-four various types of grafts supported externally by nylon net for periods up to 301 days. Of seven control grafts studied in excess of thirty days, there has been moderate to marked dilatation in six.

CLINICAL MATERIAL

Encouraged by the tolerance of tissues to the nylon netting in the experimental animal, and realizing the wide uses of this strong, elastic material, we have applied it in several human patients. They are being presented, not from the standpoint of long follow-up, but rather to suggest practical methods of application under various circumstances. In addition to the investment of vessel grafts, we have used it to support or even compress aortic aneurysms. The following cases are illustrative.

CASE 1 (035341).—M. C., a 46-year-old physician, had experienced a sudden bowel obstruction necessitating colostomy elsewhere prior to his first admission in March, 1951. An anterior resection for carcinoma of the sigmoid, partial cystectomy, and cecostomy were performed. He subsequently recovered and enjoyed good health for eighteen months. He returned because of mild abodminal pain and passage of blood per rectum. A recurrence of carcinoma in the area of the resection was found on exploration, with extension into the retroperitoneal tissues. Consequently, only colostomy was performed. The family, however, demanded that another effort be made to excise the growth, which seemingly had not metastasized. On Nov. 24, 1952, exploration revealed that the localized tumor mass invested the left external iliac artery. We joined in the operation, since resection of the



A. *B.*

Fig. 5.—*A*, An autologous pericardial tube supported by nylon net implanted in the thoracic aorta of a dog for 215 days.

B, An unsupported pericardial autograft, implanted for 206 days into the thoracic aorta of a dog. Note the dilatation and irregularity.

vessel seemed necessary. A 5 cm. segment of iliac artery about which the tumor grew was resected, and a 4.5 cm. length of left superficial femoral vein was used as a graft. A jacket of nylon net was sewn about the graft so as to diminish the size to match that of the adjacent artery. Also, it was fixed to the artery beyond the anastomoses so as to reduce the tension on the suture lines. Blood flow was very satisfactory. Subsequently, during the mobilization of the mass from the sacrum, severe bleeding from pelvic vessels necessitated packing this area and abandoning the operation. During the subsequent two weeks, the pack was partially withdrawn, with intermittent bleeding. On the thirteenth day after removal of the packs, secondary hemorrhage occurred with death of the patient. During the entire period the reinforced graft functioned satisfactorily, since both femoral pulses were strong and equal. No autopsy was performed.

CASE 2 (136471).—G. C., a 60-year-old white man, was admitted April 23, 1953, complaining of left flank pain of six months' duration. Urologic studies in another hospital during a recent severe attack had excluded calculus, but did show angulation of the ureter. A pulsatile mass, felt under the lateral left costal margin, was diagnosed as saccular arteriosclerotic aneurysm of the abdominal aorta. The confirming aortogram revealed a 5 cm. sac, arising immediately below the renal arteries. On April 27, 1953, the aneurysm was exposed through a left thoracoabdominal incision. The sac and a 7 cm. segment of aorta were resected and replaced by a matching preserved aortic homograft. The graft and adjacent aorta were invested snugly by a triple layer of nylon net. In addition, a bilateral lumbar sympathectomy was performed. Postoperative aortogram revealed a satisfactory patent graft. The peripheral pulses have remained strong, and the patient has recovered completely (Figs. 6, *A*, *B*, and *C*).

Fig. 6*A* (Case 2).—A saccular arteriosclerotic aneurysm of the abdominal aorta originating immediately below the renal arteries. The sac appears below the left renal vein and presents to the left of the aorta.

Comment.—In these two patients, grafts were implanted as in the experimental series, with external support by nylon netting. The first patient with a vein graft died presumably from the same source of bleeding as that which necessitated the large gauze roll packing. Without an autopsy, it cannot be proved that the graft remained intact, but good pulses were obtained during the entire postoperative period. The second patient with a preserved aortic homograft has done very well. It is anticipated that the graft is well protected against any possibility of the development of dilatation or aneurysm, such as has been observed in animals with long-term follow-up.

Realizing that the great strength and elastic qualities of the nylon netting should serve to permit safe reduction of the diameter of aneurysms by external compression, we have used it in two cases of aneurysm of the thoracic aorta.

B. *C.*

Fig. 6, *B* and *C* (Case 2).—*B*, Appearance of the preserved aortic homograft after resection of the aneurysm. The slight angulation results from extra length which was planned so as to reduce tension on the suture lines.

C, The graft and adjacent aorta invested snugly by a triple layer of nylon net.

CASE 3 (127407).—P. M., a 61-year-old white man, had noted chest pain and shortness of breath in 1942. Roentgenogram of the chest at that time was interpreted as being negative. Films in 1947 revealed a questionable fusiform aneurysm of the descending thoracic aorta. This diagnosis appeared more secure as subsequent films up to 1953 showed marked enlargement and pulsation of the mass. Increasing chest pain, shortness of breath, and coughing led to his admission on Jan. 30, 1953. Because of hypertension and an enlarged heart, he had an extensive investigation of his cardiac and renal status. He was digitalized because of borderline failure, and he improved preoperatively. Angiocardiogram revealed a very large fusiform aneurysm arising close to the subclavian artery and ending a few centimeters above the diaphragm. On Feb. 5, 1953, a left thoracotomy was performed. Bethune tourniquets were placed about the aorta above and below the aneurysm for hemostatic control. The aneurysm, measuring 18 cm. in length by 12 cm. in diameter, was completely mobilized by division of several pairs of intercostal arteries and cautious dissection. No serious bleeding was encountered. A square of the nylon mesh was placed about the aneurysm, and a row of horizontal mattress sutures were placed so as to form a tube about the vessel and compress the segment evenly when the sutures were tied. This

resembled the action of a corset on the human torso. Two additional layers were applied, each one a bit tighter, until the final diameter of the aneurysm was 5 cm. Although it was slightly angulated, the contour was smooth. External compression appeared to thicken the wall of the aneurysm. Because of the knots at each crossing of nylon filaments, expansile pulsation of the aneurysm was preserved. The patient received three pints of blood during operation and appeared in excellent condition following surgery. However, because of a complete renal suppression his condition degenerated, and he died on the fourth day. The anuria was thought to be related to transfusion. Autopsy revealed an excellent result in so far as the aneurysm was concerned. All the distal vessels, including renal arteries, were widely patent. His history, laboratory tests, and histologic findings favored arteriosclerosis as the cause of the aneurysm.

A. *B.*

Fig. 7.—*A*, Large fusiform syphilitic aneurysm of descending thoracic aorta. A small sacculation may be seen in the mid-portion on the left.

B, Nylon net has been used in a triple layer to diminish the diameter of the aneurysm and to render effective external support.

CASE 4 (135340).—J. S., a 52-year-old Negro, complained of throbbing pain in the left chest for four years. It had become constant in the three months prior to admission on April 22, 1953. The pain was worse when he lay on the left side, and he then noted a cough with whitish sputum. The blood serology was strongly positive, although the spinal fluid was negative. His chest film revealed a rounded 3 cm. shadow projecting to the right of the ascending arch of the aorta, as well as a large fusiform aneurysm of the descending aorta, similar to that seen in Case 3. On May 12, 1953, a left thoracotomy was performed. The aneurysm measured 17 cm. long and 12 cm. wide. There were three sacculations, 2.5 cm. in diameter, one of which had occluded the bronchus to the left lower lobe. Because of anesthetic difficulties resulting from purulent secretions, and because of long standing atelectasis and consolidation, a lobectomy was performed. The aneurysm was mobilized and compressed by three layers of nylon mesh as in Case 3. The external contour was

smooth, and blood flow was unimpeded. The patient has recovered without incident, and is comfortable. A decision has not been reached regarding management of the smaller aneurysm of the ascending arch.

Comment.—These two cases were very similar anatomically, and were amenable to external compression. The unfortunate death of the first patient was thought to be unrelated to the actual surgery of the aneurysm. This is supported by the uneventful recovery in the second case. In neither was aortic blood flow interrupted. This technique would seem to hold great promise in large fusiform aneurysms of the thoracic aorta. Here, resection and grafting is difficult and hazardous, and wiring uncertain. The use of solid film or woven cloth seems less desirable because of an absence or loss of elasticity when these materials are under stretch. If these materials begin to fragment there is no limiting factor such as the many knots of the nylon net. An additional case of aneurysm is presented in order to show still another technique.

CASE 5 (115279).—C. S., a 52-year-old white man, was admitted Jan. 13, 1953, complaining of abdominal pain and constipation of four months' duration. A pulsatile mass in the midabdomen was proved by aortography to be a fusiform aneurysm of the aorta, below the renal arteries. Other studies were not significantly abnormal. On Feb. 9, 1953, the aneurysm was mobilized from its bed by division of lumbar branches and sharp dissection. Moderate blood loss occurred from the surface of the lumbar vertebrae. The aneurysm was opened by an incision in the long axis after occlusion above and below with Potts' coarctation clamps. The superficial wall appeared to be adequate aorta, whereas the lateral and posterior walls were very thin. This latter portion was oversewn, and the edges of good wall were approximated by means of mattress sutures of 000 silk, so as to fashion a new channel, 2 cm. in diameter. Nylon net was then applied externally for support. Lumbar sympathectomy was also performed. A diffuse bleeding began from all cut surfaces late in the operation and increased despite use of calcium gluconate, protamine, and vitamin K. A total of 11,000 c.c. of blood was given the day of operation, and 3,000 c.c. the next day. With the use of fresh blood, the bleeding lessened. On the following day, an additional 1,000 c.c. was administered with stabilization of vital signs. The prothrombin time was between 20 and 22.7 seconds (normal, 15 seconds) postoperatively. On Feb. 11, the platelet count was 65,000. In addition to receiving antibiotic drugs, the patient was digitalized. Nevertheless, there was a gradual deterioration with oliguria, and the patient died on the fifth day. The hemoglobin was then 13.6 Gm., and the white cell count was 6,950. It was thought that at no time did the aorta play a role in the bleeding. Unfortunately, an autopsy was not obtained.

DISCUSSION

Nylon is the generic name for a variety of polyamide resins discovered in 1928.[18] The elasticity and tensile strength are greater than those found in any other commonly used textile fiber. In the field of surgery, its greatest use has been as a suture material.[19-23] Experimental and clinical studies have shown that the nylon fiber causes little or no reaction in tissues, and appears to remain unchanged for many years in the human being. The monofilament causes less reaction than the braided form, as might be expected. Recently, Oppenheimer and co-workers[24, 25] have reported on sarcoma production by various plastic films implanted subcutaneously in cancer-susceptible rats. Up to 40 per cent of the animals developed sarcoma in eight to fourteen months when certain films were implanted. However, only one animal of a series of

twenty-one tested to date with nylon film showed a sarcoma. To our knowledge, no malignancy has ever been produced by nylon filament in human beings. The extremely low incidence of sarcoma occurring with nylon film in the rodents studied to date raises some question as to the actual importance of this finding, since sarcoma can occur in susceptible rats from implantation of glass cover slips, polyethylene, or cellophane.[26] Nonetheless, cellophane and other films have been used frequently in recent years, especially in the treatment of aneurysm.

Nylon in the form of a fabric has been used successfully, mainly in orthopedic surgery as a joint lining.[27-30] When used in moving joints, the fabric has proved to be well tolerated. The use of a nylon net for the support of tissues has been described previously.[31-34] In these reports, its use was limited largely to the repair of hernia. The results, in general, were satisfactory.

In regard to blood vessels, external support has been tried with autogenous tissues in preference to synthetic materials which would act as a foreign body. Sako[6] used fascia lata as a support to grafts in dogs. His observations of caval grafts reinforced by fascia extended over a period of one year, and those of pericardial grafts, a period of eighteen months. His results would indicate that, at least, for limited periods, this type of support was satisfactory. Wylie and associates[35] also employed fascia lata for external support of major arteries after thromboendarterectomy and aneurysmorrhaphy with favorable results. Hui and Deterling[36] fashioned grafts of fascia lata and implanted them into the thoracic aorta of dogs. There was dilatation and saccular aneurysm formation, often multiple, in animals observed for over ten months. It seems evident from the inherent nature of this type of fibrous tissue that its lack of resiliency and elasticity favors stretching in response to a continuous pulsatile force over a long period of time. The same may be said of pericardial tissue. Johnson and co-workers[16] found dilatation of venous grafts implanted in the thoracic aorta, even with external support by pericardium.

Since the long-term behavior of autogenous tissues as a buttressing material is open to some question, it seemed reasonable to evaluate synthetic material. Nylon mesh was chosen rather than a simple fabric for several reasons. First, since each fiber is knotted at its crossing, there is no shearing of tissue growing through the interstices. Second, fibroblastic growth through the wide mesh permits a more secure fixation of the material to the graft. Third, fabricating the tubes so that there is an oblique or spiral alignment of the fibers to the long axis of the vessel allows simulation of the actual disposition of the elastic lamellae in the aorta and major arteries.[37] The elasticity of the individual nylon fiber is enhanced by the nature of the weave, when so aligned. A two-way stretch is thus achieved, and permanent or progressive distortion is resisted.

Our selection of grafts was influenced by two considerations, namely, the use of grafts which might dilate rapidly and reveal early differences and the use of a graft which might well have clinical application. The external jugular vein and pericardial grafts represent the former, and the caval grafts, the

latter. In answer to our anticipations, there was a very significant dilatation noted within several months in 86 per cent of the unsupported grafts of jugular vein or pericardium. No significant dilatation was observed in any of these same grafts, when support was afforded by nylon net. A number of these dogs are being observed for prolonged periods, since as long as two years may be necessary to show dilatation or aneurysm. This has been particularly true of caval autografts.[8, 9] Nabatoff and associates found little significant alteration until after eighteen months, and then moderate to marked dilatation up to two years. After this, there was only slight change during the next year. Johnson and co-workers[3] and Coleman[38] found little increase during the first year, possibly because of the marked thickening of the wall by fibroblastic activity. After eighteen months, this thickening decreases.[39] Since as long as two years may be necessary to demonstrate significant differences in results with caval grafts, we cannot properly assess the value of nylon support of caval grafts at this time. It can be stated, however, that to date no measurable alteration has occurred. In time, we can compare the findings with control series as reported by Johnson and associates, and Nabatoff and co-workers, and as being carried out in our laboratory by Coleman.

It has been noted as well that thinning, and even aneurysm formation, does occur after eighteen months with aortic homografts. Grindlay and Seybold noted an aneurysm in an aortic homograft implanted in a dog for one year.[12] Pate and co-workers have found moderate thinning of lyophilized aortic homografts after one year.[13] Deterling and associates[14] and Hufnagel[15] have observed varying degrees of thinning in aortic homografts studied well beyond three years in dogs. These grafts had been preserved by quick freezing. Similar changes occur in fresh homografts and those preserved in a nutrient electrolyte solution.[14] Moderate dilatation and even aneurysm formation have been noted in arterial heterografts studied for one year or more.[13, 14] In summary, it can be stated that all tissue replacements in the aorta appear to undergo anatomic alterations of varying degrees in time. It is our hope that these can be eliminated by means of an elastic external support.

The desirability of smooth linear flow in blood vessel grafts has been well established. Schmitz and co-workers[11] have shown that the incidence of vascular complications can be significantly reduced by tailoring the graft to conform to the diameter of the host vessel. The nylon net provides a method of permanent tailoring of a graft in addition to supporting it and protecting the suture line by reducing tension. As a consequence, we have observed only two complications among thirty-four grafts supported by nylon net, and in no instance was there any dehiscence of an anastomosis. In one, complete thrombotic occlusion occurred as a result of constriction of the proximal suture line. In the other, a small mural thrombus was noted.

Because of its physical characteristics, the nylon net lent itself admirably to the external support and tailoring of vessels in which the wall had been damaged as a result of disease or degeneration. Our limited use of this material in the treatment of aortic aneurysms to date has been encouraging. For

maximal protection and tailoring, it is essential that the aneurysmal segment be completely encircled. Significant reduction in the size of certain aneurysms has been achieved. However, there should be a relative absence of clot and atheromatous degeneration of the wall, or peripheral embolism may occur. Even with external support alone, there would appear to be reasonable protection afforded. The most satisfactory form of treatment appears to be either aneurysmorrhaphy or excision and replacement by a graft, whenever possible.

Several other clinical applications are suggested by our study. Prevention of dilatation following thromboendarterectomy and reduction of tension or disproportion at vascular suture lines are examples. We hope that the long-term evaluation of the uses of nylon net will be as encouraging as the results to date.

SUMMARY

Nylon in the form of tulle-woven net has been used to tailor and to provide external support to blood vessels and vascular grafts. This material was used about venous or pericardial grafts in thirty-four dogs. No significant dilatation was observed over a period of nine months, whereas 86 per cent of unsupported controls revealed moderate to marked dilatation during a similar period. The nylon net was used clinically to support vessel grafts in two patients, and to tailor and support aortic aneurysms in three other cases. The results of these studies have been encouraging.

ADDENDUM

Since the presentation of this paper, we have had additional opportunity to use nylon net for external support. A long coarctation was resected in a 25-year-old man, and a 6 cm. graft of preserved human aorta was used to bridge the defect. The lower portion of the graft had a greater diameter than the host aorta, and it was possible to achieve perfect alignment by means of a double layer of nylon net sewn about the graft and adjacent host aorta.

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said that whatever is the ultimate cause, there can be little doubt that the proximate mechanisms are physical, namely, the laws that govern fluids in motion (hydraulics). The flow of blood is dependent upon the same three factors that control the motion of all enclosed fluids, namely, the head of pressure, the peripheral resistance, and the viscosity of the fluid itself.

Change in the viscosity of the blood does not appear to be of significance in the production of ischemic necrosis under ordinary circumstances, although it may be of importance in the ischemia produced by exposure to profound cold, and possibly may be of importance in adding to the ischemia in a limb that is cold because of obliterative arterial disease. How this capacity for change in viscosity of the blood could be turned to advantage (if possible at all) in our efforts to form or improve the collateral arterial circulation remains obscure.

The remaining two factors operative in hydraulics, the head of pressure and the peripheral resistance, must be taken into consideration as the mechanisms that increase local blood flow to an extremity with obliterative arterial disease. And they can only be considered in their relation one to the other. For example, gangrene may occur in the digits of a patient with marked hypertension while the tissues may be amply nourished when the blood pressure is deliberately maintained below so-called "shock" levels during hypotensive anesthesia. Given, however, a fixed peripheral resistance, the blood flow will vary with changes in head of pressure, and vice versa.

Logically, then, the total blood flow to an ischemic extremity could be increased if the systemic pressure could be elevated without a corresponding increase in the peripheral resistance in the limb. The chief difficulty with this approach to the problem is the fact that sympathomimetic drugs that elevate blood pressure do it, partially at least, by peripheral vasoconstriction. There is evidence that ephedrine does not act directly on the effector organ but produces its effect by inhibiting the enzymatic destruction of the substance liberated by adrenergic nerves,[16, 17] much as eserine inhibits the destruction of acetylcholine. If this is correct, ephedrine and similarly acting substances might be expected to increase the blood flow in an extremity following sympathetic ganglionectomy. The effect on the heart and vessels of the rest of the body would remain, but there would be no action on the denervated vessels in the absence of circulating adrenaline. In an isolated experiment on a patient who had a lumbar sympathectomy for obliterative arterial disease, evidence has been observed suggesting that blood flow to the extremity was increased by such a method.[9] It is planned to pursue this further, although it is recognized that it would be inadvisable to elevate the systemic blood pressure in many patients with obliterative arterial disease.

To date, the most practical approach to the problem of increasing blood flow to an extremity with obliterative arterial disease has been the attempt to reduce the peripheral resistance to the flow of blood, thereby, assuming a relatively fixed head of pressure, increasing the rate of flow. The most popular method of doing this has been by lumbar sympathectomy, which produces

a permanent state of vasodilatation. On the basis of available evidence, it is not possible to say whether or not ganglionectomy affects the diameter of the collateral arteries directly. It does, however, dilate the arterioles of the skin and, most probably, it dilates the arteriovenous shunts. Thus, the increased blood flow may not be all nutritive, some being shunted back into the venous system without traversing the capillaries, but, in any case, there is an increased rate of blood flow through the collateral vessels in response to the decrease in peripheral resistance. In dogs, this increase in rate of blood flow through the femoral artery was found to be twice the rate of the normally innervated side by Herrick, Essex, and Baldes.[21] Clinically, it appears that the nutrition of the extremity increases slowly and steadily with the passage of time following lumbar sympathectomy, even though the maximum rise in skin temperature may be found within the first forty-eight hours after operation. It is possible that the collateral arteries dilate secondarily in response to an increased velocity of blood flowing through them, which may also be one of the important contributing factors causing the dilatation that occurs in the proximal artery of an arteriovenous fistula.

Another approach to the problem of increasing blood flow to an ischemic extremity by decreasing the peripheral resistance to the flow of blood has been the use of changes in the environmental pressure. The logic of this approach was evident in the seventeenth century. Indisputable proof, however, of the actual value of the method as used up to this time has been difficult to obtain. Passive vascular exercises have been given an extensive trial at the Cincinnati General Hospital during the past twenty years, but accurate appraisal of results has been handicapped in this clinic, as well as other clinics, by the lack of objective methods in evaluating the state of the peripheral circulation in health or disease. Clinically, some patients have been greatly benefited. The improvement occurred at a more rapid rate and to a far greater degree than could be expected by spontaneous development of collateral arterial pathways. On some patients, passive vascular exercises had no detectable effect and, as might be expected, in many instances it was not certain whether the improvement resulted from exposure to changes in environmental pressure, the general care of the extremity, spontaneous development of collateral arterial pathways, or a combination of all these factors. The most striking improvement was noted in patients with sudden arterial occlusion or with obliteration of the major arteries with evidence of motor activity. In extremities with advanced arteriolar obliteration, significant improvement cannot be expected by this method or by lumbar sympathectomy.

Prior to World War II, a cylinder had been developed in which both lower limbs and the pelvis could be enclosed. It was thought that by using intermittent negative pressure in such a chamber more benefit could be obtained than by using the pavaex boot, which enclosed only the leg and distal third of the thigh. By enclosing a larger area, it should be possible to enlarge the collateral arterial pathways of the thigh and pelvis. Unfortunately, this work had to be discontinued due to the exigencies of the critical period, and could not be pursued further until this past year. Technical difficulties have

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EVALUATION OF FACTORS WHICH INFLUENCE THE CIRCULATION IN EXTREMITIES WITH OBLITERATIVE ARTERIAL DISEASE

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A PATIENT complains of pain in the calves of the legs that is brought on by walking and is relieved by standing still. No other symptoms can be elicited. On examination, the feet and legs are warm and dry. The texture of the skin is good, and there is atrophy neither of the subcutaneous tissue nor of the muscles. Pallor does not appear when the feet are elevated above the level of the heart nor is there rubor of the toes on pendency. The arterial circulation of the legs and feet appears to be adequate and, barring injury or infection, there is no danger of gangrene. The pulses, however, are not palpable below the aorta.

This is a clinical picture not infrequently encountered in practice. If those patients in whom the occlusion starts in the common femoral artery are included, it is quite common.

When treating such patients, a clear distinction must be made between the pathologic process within the major arteries and the over-all arterial blood supply of the extremity. Pathologically, arteriosclerosis obliterans is considered an irreversible, progressive process that encourages intra-arterial thrombosis and terminates with complete obliteration of the involved arteries. Granted that the clinician may be unable to halt the progressive obliteration of the major arteries, he can do a great deal to safeguard and actually improve the over-all circulation of the extremity, since in most cases the secondary or collateral arteries are not significantly involved by this degenerative process of the major arteries.

Just as, when treating an elderly patient with a fractured humerus, the orthopedic surgeon is more concerned with the functional result than with the anatomic result as demonstrated by an x-ray film,* so too the clinician treating a patient with obliterative arterial disease must focus his attention on the stimulation of the collateral arterial circulation rather than on the underlying pathologic process affecting the major arteries.

Although pathologically irreversible, major arterial obliteration results in gangrene only if the collateral arteries are insufficiently developed to provide the necessary nourishment. Therefore, the clinician should direct the therapy toward improving the efficiency of the secondary circulation, and in this way

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*An x-ray film may show an anatomically perfect reduction of the fragments of bone while the patient has lost all use of the arm, or it may show poor alignment of the fragments while the patient has regained tolerable or even full use of the involved extremity.

relieve symptoms of ischemia and prevent the occurrence of gangrene, rather than attempt to remove a localized obstruction in the major arterial system which is diffusely involved in the obliterative process.

Collateral arteries may be defined as accessory macroscopic secondary arteries that are in continuity, directly or indirectly, with the major arterial trunk proximally and, sometimes, distally. When fully developed, these vessels form an extensive network that can be visualized radiographically (Fig. 1). As previously stated, there is clinical proof that these vessels can maintain the circulation in spite of complete occlusion of the major arteries to the extremity. It is, however, not easy to furnish objective proof that any form of therapy directly stimulates the formation of new pathways or enlarges those which are already present. Nor can we clearly identify the mechanisms responsible for this development when it occurs.

Fig. 1.—Radiograph demonstrating the extent of the collateral arterial circulation in the foot of a patient who had complete obliteration of the major arteries. This patient had been treated by pavaex for 106 hours. (From Herrmann, L. G.: Passive Vascular Exercises, J. B. Lippincott Company.)

In general, it may be said that there are two basic schools of thought concerning the ultimate stimulus for development or improvement of the collateral arterial circulation. One group believes that the stimulus comes from the accumulation of tissue metabolites in the area of the body in which the circulation is diminished.[4, 32, 50] The other group teaches that practically all changes in the arterial tree secondary to ischemia may be explained in purely physical terms.[23-25] Without entering into this controversy, it can safely be

said that whatever is the ultimate cause, there can be little doubt that the proximate mechanisms are physical, namely, the laws that govern fluids in motion (hydraulics). The flow of blood is dependent upon the same three factors that control the motion of all enclosed fluids, namely, the head of pressure, the peripheral resistance, and the viscosity of the fluid itself.

Change in the viscosity of the blood does not appear to be of significance in the production of ischemic necrosis under ordinary circumstances, although it may be of importance in the ischemia produced by exposure to profound cold, and possibly may be of importance in adding to the ischemia in a limb that is cold because of obliterative arterial disease. How this capacity for change in viscosity of the blood could be turned to advantage (if possible at all) in our efforts to form or improve the collateral arterial circulation remains obscure.

The remaining two factors operative in hydraulics, the head of pressure and the peripheral resistance, must be taken into consideration as the mechanisms that increase local blood flow to an extremity with obliterative arterial disease. And they can only be considered in their relation one to the other. For example, gangrene may occur in the digits of a patient with marked hypertension while the tissues may be amply nourished when the blood pressure is deliberately maintained below so-called "shock" levels during hypotensive anesthesia. Given, however, a fixed peripheral resistance, the blood flow will vary with changes in head of pressure, and vice versa.

Logically, then, the total blood flow to an ischemic extremity could be increased if the systemic pressure could be elevated without a corresponding increase in the peripheral resistance in the limb. The chief difficulty with this approach to the problem is the fact that sympathomimetic drugs that elevate blood pressure do it, partially at least, by peripheral vasoconstriction. There is evidence that ephedrine does not act directly on the effector organ but produces its effect by inhibiting the enzymatic destruction of the substance liberated by adrenergic nerves,[16, 17] much as eserine inhibits the destruction of acetylcholine. If this is correct, ephedrine and similarly acting substances might be expected to increase the blood flow in an extremity following sympathetic ganglionectomy. The effect on the heart and vessels of the rest of the body would remain, but there would be no action on the denervated vessels in the absence of circulating adrenaline. In an isolated experiment on a patient who had a lumbar sympathectomy for obliterative arterial disease, evidence has been observed suggesting that blood flow to the extremity was increased by such a method.[9] It is planned to pursue this further, although it is recognized that it would be inadvisable to elevate the systemic blood pressure in many patients with obliterative arterial disease.

To date, the most practical approach to the problem of increasing blood flow to an extremity with obliterative arterial disease has been the attempt to reduce the peripheral resistance to the flow of blood, thereby, assuming a relatively fixed head of pressure, increasing the rate of flow. The most popular method of doing this has been by lumbar sympathectomy, which produces

a permanent state of vasodilatation. On the basis of available evidence, it is not possible to say whether or not ganglionectomy affects the diameter of the collateral arteries directly. It does, however, dilate the arterioles of the skin and, most probably, it dilates the arteriovenous shunts. Thus, the increased blood flow may not be all nutritive, some being shunted back into the venous system without traversing the capillaries, but, in any case, there is an increased rate of blood flow through the collateral vessels in response to the decrease in peripheral resistance. In dogs, this increase in rate of blood flow through the femoral artery was found to be twice the rate of the normally innervated side by Herrick, Essex, and Baldes.[21] Clinically, it appears that the nutrition of the extremity increases slowly and steadily with the passage of time following lumbar sympathectomy, even though the maximum rise in skin temperature may be found within the first forty-eight hours after operation. It is possible that the collateral arteries dilate secondarily in response to an increased velocity of blood flowing through them, which may also be one of the important contributing factors causing the dilatation that occurs in the proximal artery of an arteriovenous fistula.

Another approach to the problem of increasing blood flow to an ischemic extremity by decreasing the peripheral resistance to the flow of blood has been the use of changes in the environmental pressure. The logic of this approach was evident in the seventeenth century. Indisputable proof, however, of the actual value of the method as used up to this time has been difficult to obtain. Passive vascular exercises have been given an extensive trial at the Cincinnati General Hospital during the past twenty years, but accurate appraisal of results has been handicapped in this clinic, as well as other clinics, by the lack of objective methods in evaluating the state of the peripheral circulation in health or disease. Clinically, some patients have been greatly benefited. The improvement occurred at a more rapid rate and to a far greater degree than could be expected by spontaneous development of collateral arterial pathways. On some patients, passive vascular exercises had no detectable effect and, as might be expected, in many instances it was not certain whether the improvement resulted from exposure to changes in environmental pressure, the general care of the extremity, spontaneous development of collateral arterial pathways, or a combination of all these factors. The most striking improvement was noted in patients with sudden arterial occlusion or with obliteration of the major arteries with evidence of motor activity. In extremities with advanced arteriolar obliteration, significant improvement cannot be expected by this method or by lumbar sympathectomy.

Prior to World War II, a cylinder had been developed in which both lower limbs and the pelvis could be enclosed. It was thought that by using intermittent negative pressure in such a chamber more benefit could be obtained than by using the pavaex boot, which enclosed only the leg and distal third of the thigh. By enclosing a larger area, it should be possible to enlarge the collateral arterial pathways of the thigh and pelvis. Unfortunately, this work had to be discontinued due to the exigencies of the critical period, and could not be pursued further until this past year. Technical difficulties have

been encountered, and it is impossible to say at this time whether or not this method will prove to be of practical value. Preliminary observations, however, suggest that it may be more effective than the application of alterations of environmental pressure only to the distal half of an extremity.

Clinically, the use of intermittent venous occlusion, while of no apparent benefit to patients with chronic arterial insufficiency, seems to be of value in the treatment of acute arterial insufficiency. This is in accord with the findings of Collens and Wilensky[5, 6] and Linton.[34] On the other hand, Gregg, Pritchard, and Shipley[20] and Thompson[62] have demonstrated that this procedure does not increase the rate of blood flow to the limb of the experimental animal. This apparent discrepancy may be explained by the fact that the nutrition of the tissues, which is the primary concern of the clinician, is affected by other factors in addition to the rate of blood flow. Distention of the capillaries with blood and the length of time the blood remains within the capillary loops are factors that likewise must be considered.

Landis[30, 31] has demonstrated that human capillary pressure is directly related to venous pressure. Reduction of the venous pressure in the limb with obliterative arterial disease by elevation causes the capillaries to empty within a short period of time, as is evidenced by the appearance of a cadaveric color. In order for the capillaries to be filled, the total inflow of blood must approximate total outflow. Obviously, this is impossible when the limb with arterial insufficiency is elevated, because the capacity of the veins to drain the capillaries is relatively normal while the function of the arterial system has been reduced to a fraction of its normal capacity by the obliterative process. The capillaries, however, are engorged when the limb is pendent. In all probability, this gravitational drainage when the limb is elevated accounts for the pain that so frequently occurs in the toes and metatarsal areas of the foot when a patient with advanced obliterative arterial disease rests in bed. The relief of pain that is obtained when he sits, stands, or elevates the head of the bed is probably due to the fact that the capillaries are filled with blood caused by elimination of the gravitational effect on the venous outflow. Accordingly, it seems reasonable to conclude that the engorgement of the capillaries by intermittent venous occlusion, even though the over-all rate and volume of arterial blood remain the same or are diminished, permits a greater transfer of nutritive products to the tissues than when the capillaries are practically empty.

Before considering the merits of the individual vasodilator drugs in the treatment of peripheral obliterative arterial disease, it is worth while to review some of the variables that make proper evaluation of any type of therapy for this condition very difficult.

The first variable is the nature of the disease. Contrary to popular opinion, the clinical course of the disease is not a straight-line progression and does not inevitably lead to gangrene. True, the pathologic process within the major arteries progresses toward complete obliteration of the artery, but this is a stepwise rather than an uninterrupted march. In fact, at any time the

total effective blood flow may level off or even improve as the collateral pathways enlarge. Since it is frequently impossible to distinguish between the improvement that occurs spontaneously and that which results from treatment, it is hazardous to attribute improvement to a specific agent or method of treatment being used at that time. Furthermore, a patient is usually given the benefit of several forms of therapy simultaneously, and there is a tendency to minimize the contribution made by the collateral efforts and to maximize the benefit of the particular agent in which the clinician happens to be interested. For example, it is easy to underestimate the value of careful foot hygiene and bed rest and to overemphasize benefit obtained from various vasodilator drugs.

The second variable is the fact that the degree of the disease, whether maximal or minimal, must be taken into consideration when trying to produce vasodilatation in the lower extremities. Even in normal subjects, it is more difficult to effect vasodilatation in the toes than in the fingers.[11, 27, 45] This can be noted when the body is warmed to produce vasodilatation in the extremities and also when a drug such as nicotinic acid or its derivatives is used. It produces a subjective sensation of warmth in the face and upper extremities but has no significant vasodilator action on the arterioles of the normal lower extremity.[53]

The difficulty in producing vasodilatation in the lower extremities is greatly magnified in the presence of obliterative arterial disease. Elkin and Cooper[14] noted no rise in skin temperature or digital pulsations of toes with obliterative arterial disease, even though the more normal opposite extremity did show evidence of improved arterial circulation when Priscoline was administered. Indeed, patients with advanced obliterative arterial disease of the lower extremities have been observed in whom the temperature of the toes could not be elevated by immersion of the hands and forearms in water at 107° F. for two hours, or after blocking the tibial nerve at the ankle with procaine.[8] Only following lumbar sympathectomy were significant rises in skin temperature noted. This demonstrates clearly the inherent difficulty of producing vasodilatation in the extremity with obliterative arterial disease and should underscore the skepticism with which must be viewed claims of improved circulation in such patients following the use of various vasodilator drugs.

Still another factor to be borne in mind is the possible harmful effects of any agent that produces a generalized vasodilatation on a patient with advanced obliterative arterial disease of the lower extremities. If the agent is efficient enough to dilate the blood vessels, it will have its maximum effect on those areas of the body in which the vessels are more nearly normal, and a minimal effect on the area in which the greatest effect is desired. In fact, the inability of the vascular bed of the diseased extremity to expand in proportion to the more normal areas of the body may bring about a detrimental shifting of blood.[49]

Another important variable is the part played by local bacterial infection, if present. The growth of bacteria competes with the tissues for the available

oxygen; if it is uncontrolled, the tissues will be deprived of the previously adequate, although greatly reduced, nourishment. On the other hand, a near-gangrenous toe may become perfectly viable following elimination of the infection. No one underestimates the value of properly selected antibiotic substances in the treatment of such infections but, again, the real benefit of the bed rest is frequently overlooked. As an illustration, a case is briefly presented.

An 80-year-old man with advanced obliterative arterial disease of the lower extremities was seen in consultation. There were no palpable pulses below the femoral arteries, and the left great toe was swollen and erythematous except for the distal third, which was covered with black and gray purulent material. He had had his great toenail removed, and the tissues became infected. The problem appeared to be whether or not a supracondylar amputation would be necessary, or whether it might be possible to remove the toe and the head of the first metatarsal. He was admitted to a hospital and treated by bed rest and warm saline compresses every six hours for two days while awaiting the laboratory report of the type of organisms grown on culture. The saline compresses were then omitted. By the time the report was obtained, in seventy-two hours, all swelling and erythema had disappeared. The toe was dry and the nail bed was covered by a dry eschar. Improvement continued, and he was instructed in active vascular exercise and discharged from the hospital in seven days.

Had antibiotic substances been used, the dramatic improvement would certainly have been attributed to them.

Finally, clinical evaluation of therapeutic improvement on the basis of subjective testimony by the patient is likely to be woefully misleading. In this connection, it would be interesting to note that in an unpublished study of the effectiveness of a vasodilating agent in the treatment of patients with obliterative arterial disease of the lower extremities, no correlation could be found between subjective improvement as reported by the patient and objectively measured increased functional capacity, that is, increased ability to walk continuously at a controlled rate, the ability of muscles of an individual extremity to contract against an increasing resistance, changes in the skin temperature, or amplitude of the digital pulsation of the toes under controlled conditions.[10]

Being aware of these pitfalls, a careful review of the literature was made for objective evidence that would demonstrate whether or not the various vasodilating drugs can produce their effect on vessels of the human lower extremity with obliterative arterial disease. Since clinical evaluation is so uncertain, attention was directed to those investigations in which laboratory methods were used. True enough, the laboratory methods themselves at times are open to criticism but, under certain conditions, some positive information can be obtained which is more trustworthy than clinical impressions alone.

For ease of presentation, the drugs will be divided into three groups. The first includes those drugs which may have a vasodilating effect on the vessels of some portions of the body, but which have no effect, or an insignificant effect, on the circulation of the normal lower extremity, and therefore could not be expected to be effective in the treatment of obliterative arterial disease in lower extremities. This group includes: papaverine, pancreatic

extracts, calcium gluconate, thiamine hydrochloride, dioxyline phosphate, nicotinic acid, Roniacol Tartrate, aminophylline, "SKF 688 A,*" sodium salicylate, hypertonic saline solution, and ACTH.[12, 18, 26, 35, 43, 44, 53, 55]

The second group includes drugs which produce vasodilatation in the normal lower extremity but which have an inconstant or insignificant effect on the vessels of lower extremities with obliterative arterial disease. Alcohol, Priscoline, the tetraethylammonium ion, and hexamethonium ion are drugs of this type.

The third group includes histamine (intra-arterial) and the estrogenic hormones, which may have a beneficial effect on the circulation of the extremities with advanced obliterative arterial disease by a mechanism that is as yet not completely understood.

By means of an ingenious animal preparation, Siems and Rottenstein[58] demonstrated that ethyl alcohol produces vasodilatation in the extremity by a central action mediated through the vasomotor nerves. Horton, Roth, and Adson[27] noted that a given dose of ethyl alcohol has a more marked effect on the vessels of the face and upper extremity than on the vessels of the lower extremity in man. Several investigators have observed that its effectiveness is significantly diminished in extremities with obliterative arterial disease.[2, 7, 27, 54]

Priscoline, acting peripherally,[37, 58] produces vasodilatation in the normal lower extremity.[12, 14, 18, 37, 44, 55, 63] Its effect, however, is diminished or is absent in patients with obliterative arterial changes depending on the degree and advanced nature of the obliterative process.[12, 14, 19] Elkin and Cooper[14] and Murphy, McClure, Cooper, and Crowley[44] noted that Priscoline is not nearly as effective as novocain block of the posterior tibial nerve in producing vasodilatation in the lower extremity. Van Itallie and Clarke[63] found body heating and Priscoline roughly comparable in their effects on blood flow. Rottenstein and associates[55] concluded that the digital cutaneous blood flow produced by Priscoline was about one-half that produced by a combination of heat and food. It has been demonstrated[11] that body heating is ineffective in comparison with block of the tibial nerve or lumbar sympathetic ganglionectomy in producing vasodilatation in lower extremities with obliterative arterial disease.

The tetraethylammonium ion produces generalized vasodilatation and increases the rate of blood flow in the lower extremity as measured by the venous-occlusion limb plethysmograph.[26] It has a powerful effect on the autonomic ganglia[3] and has more recently been shown to have a peripheral vasodilator action also.[58] Its effectiveness, however, in lower extremities with obliterative arterial changes is undependable and inadequate when compared with block of the tibial nerve.[46, 47] The hexamethonium ion is also a powerful blocking agent of sympathetic ganglia and produces vasodilatation in the normal lower extremity, but it is much less effective in an extremity with

*N-phenoxyisopropyl-n-benzyl-B-chlorethylamine hydrochloride.

obliterative arterial changes.[15, 28, 57] With either of these chemical agents, a profound fall in blood pressure may occur, causing a deleterious shifting of blood away from the extremity in which the increase in blood flow is desired.

Mufson[41] has advocated the use of intra-arterial histamine in the treatment of obliterative arterial disease of the lower extremities. He noted significant clinical improvement following its use, and his findings were confirmed by the studies of Dixon, Scott, and Epstein[13] and Mackey.[38] As a means of testing its effect objectively, Mufson used changes in skin temperature of the toe and the accumulation of radioactive sodium in the extremity following its injection into an arm vein as the chief criteria of effectiveness. He recorded skin temperatures by noting the local differences and correcting them to the spontaneous changes in the opposite leg. For example, if there is a local rise of 1° C. on the foot being treated and a drop of 2.0° C. on the control foot, the final change on the treated side is recorded as +3° C. Mufson stated that this timesaving method obviates the necessity for controlled temperature rooms. This method is definitely open to criticism. It would seem that the change in local temperature of the treated extremity is the important thing to be observed and for this change to have meaning, the local environment, at least, must be controlled. This method multiplies by three the effect of the drug on the extremity being treated in the example given.

The measurement of the local accumulation of radioactive sodium in the diseased extremity as a measure of blood flow appears to give valid information when the results are negative, but the data must be interpreted with caution when a positive effect is shown. Mufson[42, 43] noted no change in radioactive sodium uptake after the administration of papaverine (16 mg.), tetraethylammonium chloride (500 mg.), aminophylline (200 mg.), and hypertonic saline solution. It can be said with confidence, then, that these agents caused no significant alteration in the local blood flow. However, an increase in radioactive sodium uptake following the intra-arterial injection of histamine does not necessarily indicate an increased rate of blood flow to the area of the extremity being measured, because the effect might be produced by any one of, or a combination of, three factors, namely, an increased rate of blood flow through the arterioles, increased capillary permeability, or increased venous stasis. Lewis[33] stressed the fact that the direct action of histamine is on the "minute" vessels, which he defines as the most distant arterioles, capillaries, and venules. The arterioles he spoke of are not the arterioles containing a large muscular coat, which is usually referred to in the American literature. Weiss, Robb, and Ellis[64, 65] concluded that histamine has a greater effect on the veins and venules of man than on the arterioles and capillaries. They pointed out that the flush following injection of histamine may be due to engorgement of the subpapillary venules and to a lesser degree of the capillary bed. Stead and Warren[59] have demonstrated that histamine intra-arterially increases the capillary permeability in man. As in the case of intermittent venous occlusion and estrogenic hormones, this capillary dilatation may be beneficial to certain patients with advanced obliterative arteriolar disease.

Dixon, Scott, and Epstein[13] noted a striking similarity between the hemodynamic response to intra-arterial histamine and to the establishment of an arteriovenous fistula, and discussed the possibility that the effect of intra-arterial histamine is to open the arteriovenous shunts, thus promoting development of the collateral circulation. Certainly, all will agree that any method offering such promise should be investigated more fully. Nevertheless, that collateral vessels will develop in response to an agent the action of which is extremely transitory and a substance which is almost immediately destroyed in the body taxes the imagination somewhat.

Estrogenic hormones have been shown to cause dilatation of the capillaries in animal experiments.[22, 39, 40, 52] This dilating action is presumably due to the liberation of acetylcholinelike compounds in the tissues.[51] The hormones have been found to be effective in preventing gangrene produced by the administration of ergot to female rats.[22, 39, 40, 48, 52, 60] However, these observations were not confirmed by all investigators of the substances.[29, 36, 61] In the human being, color changes in the digits following administration of synthetic estrogens suggest that the minute venules and capillaries are dilated, but laboratory evidence that the rate of blood flow is increased following administration of the hormone is lacking.[1] Clinically, injection of the synthetic hormone (estradiol dipropionate), in doses of 1 mg. intramuscularly three times a week, seems to be of some value in the treatment of some patients with advanced arteriolar disease in whom neither lumbar sympathetic ganglionectomy nor passive vascular exercises have a significant beneficial effect. A possible explanation is that the tissues receive more oxygen when the blood remains in the capillaries for a longer period of time than when the capillaries are collapsed. This explanation is similar to the one proposed for the apparent value of intermittent venous occlusion and might also explain the clinical improvement noted following intra-arterial administration of histamine. Indisputable proof, however, of the value of estrogenic hormones in the treatment of patients with obliterative arterial disease of the lower extremities is yet to be forthcoming.

DISCUSSION

When evaluating the efficacy of various medicaments for the treatment of obliterative arterial disease in the lower extremity, it is necessary to keep in mind some of the pitfalls that are likely to lead to erroneous conclusions. In the first place, vasomotor tone is higher in the lower extremity than in the upper extremity or in the face. Therefore, flushing of the face or hands must not be taken as evidence that the particular chemical produces vasodilatation in the feet. Second, it is much more difficult to bring about vasodilatation in the extremity with obliterative arterial disease than in the normal extremity. That is why a drug may appear to be highly effective when tried on normal extremities and have an inconstant or negligible effect on the circulation of a diseased extremity. Third, any method, physical or medicinal, that produces widespread vasodilatation will have a greater effect on those areas of the body in which the blood vessels are more nearly normal than in an extremity with

obliterative arterial disease and, if the blood pressure cannot be maintained in the presence of a reduced peripheral resistance to the flow of blood to the rest of the body, a marked shift of blood away from the extremity under treatment may occur. It is true that the blood flow may be increased to all parts of the body simultaneously in the normal individual and for brief periods in the patient with generalized arteriosclerosis obliterans,[11] yet it seems most unlikely that it will ever be possible to produce a long-lasting vasodilatation in an extremity with advanced obliterative arterial disease by any method that causes widespread vasomotor paralysis.

Clinically, patients with obliterative arterial disease of the lower extremities may be divided in two groups. In one group are those who have sufficient symptoms and signs to establish the diagnosis but whose over-all circulation is adequate and who are in no immediate danger of gangrene. The second group includes those who have advanced obliterative arterial disease and whose limbs are in a precarious state. It is almost impossible to evaluate the benefit derived from any particular agent in the treatment of patients in the first group on clinical grounds alone, because of the many variables mentioned previously. It is the patients of the second group, the critical cases which require a highly potent therapeutic agent, that we are considering here, and it is in these instances that the various vasodilating medicaments under discussion are so completely ineffectual. Certainly, there is no medicinal agent currently available whose effectiveness in producing vasodilatation in the extremity with obliterative arterial disease can approach that of lumbar sympathetic ganglionectomy.

SUMMARY AND CONCLUSIONS

1. The existence of patients with minimal evidence of arterial insufficiency despite complete occlusion of the major vessels of the lower extremity demonstrates the potential efficiency of the collateral arterial circulation and demonstrates as well that, clinically speaking, arteriosclerosis obliterans does not invariably lead to complete ischemia, but, instead, the circulation of the limb may even improve as the collateral circulation is developed. Since this is so, it seems best to direct the attention to methods of increasing the efficiency of the collateral circulation rather than to attempts to remove or by-pass localized areas of obstruction in an arterial tree which is diffusely involved in the obliterative process.

2. The proximate mechanisms affecting blood flow to an extremity are concerned with the laws of hydraulics and are governed by the head of pressure, peripheral resistance, and the viscosity of the blood.

3. At the present time, attempts to decrease the peripheral resistance to the flow of blood offer the greatest promise in the treatment of the patient with obliterative arterial disease of the lower extremities.

4. It is more difficult to produce vasodilatation in the normal lower extremity than in the normal upper extremity, and most difficult to bring about vasodilatation in the extremity with obliterative arterial disease. This ex-

plains why the various vasodilating agents under discussion are ineffectual in the treatment of patients with advanced obliterative arterial disease of the lower extremities.

5. Intermittent venous occlusion, intra-arterial histamine, and estrogenic hormones may be of some value in the treatment of certain cases of obliterative arterial disease of the lower extremity, possibly due to engorgement of the capillaries with blood.

6. There is clinical evidence that passive vascular exercises are of definite benefit to some patients with obliterative arterial disease, and it may be possible to increase the effectiveness of this type of therapy by enclosing a greater area of the body within the negative pressure chamber.

7. Lumbar sympathetic ganglionectomy is the most effective means available for the production of a long-acting peripheral vasodilatation in patients with obliterative arterial disease of the lower extremity. This vasodilatation selectively reduces the resistance to the flow of blood in the area of the body in which an increased blood flow is most needed. At the present time, it cannot be said whether or not it affects the collateral arteries directly, but there is clinical evidence that the nutrition of the tissues improves significantly with the passage of time following operation. Thus, it is most probable that in some way it favors the development of the collateral arterial circulation.

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THE PRESENT STATUS OF THE SURGERY OF MITRAL AND AORTIC STENOSIS

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THE patient with disabling rheumatic heart disease may have one or more of the cardiac valves involved in such a way as to interfere with function. At the present time, stenosis of the mitral and aortic valves can be attacked surgically with considerable success. The problem of mitral stenosis was first extensively investigated one-quarter of a century ago by Cutler, Levine, and Beck.[1] Their efforts were abandoned because of an early high mortality. There have been many advances in surgery and anesthesia since that time. The concept of avoiding regurgitation by opening the fused commissures of the mitral valve by finger fracture or with a knife, as advocated by Bailey[2] and Harken,[3] rather than by cutting away a portion of the valve has undoubtedly been the major contribution in the procedure currently used.

More recently a similar concept has been applied to the aortic valve.[4] The two problems will be discussed separately. Regurgitation of these valves is still a major problem, and it is being investigated by several workers.

MITRAL STENOSIS

The Selection of Patients.—The problem of selecting patients for mitral commissurotomy has been investigated by many cardiologists. The difficulty of deciding whether or not a given patient should be subjected to mitral surgery varies widely among individual patients. The decision may be quite easy in young patients with obvious signs of "pure" mitral stenosis and with severe symptoms. The difficulty increases when it is necessary to evaluate the effects of other factors which complicate the problem in many patients. Certain of these complicating factors will be discussed.

1. Age in itself should not contraindicate operation when the patient has significant disability arising primarily from mitral valvular obstruction. The risk is naturally greater in older patients, but the benefits achieved have been worth while in many instances. Our oldest patient was 62 years of age, and has had one of the best results in the series.

2. Most cardiologists agree that patients with rheumatic activity should not be operated upon. Activity, however, may be difficult to recognize. We

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believe that any vague illness in patients with rheumatic heart disease should be considered as evidence of activity until proved otherwise. Febrile episodes, joint or muscle pains, fatigue, malaise, and anorexia are all possible manifestations of activity. A sudden increase in the degree of cardiac disability may represent rheumatic activity. The most useful laboratory indication is an increased sedimentation rate not otherwise explained.

3. An important question is whether or not surgery should be considered in the presence of congestive failure. Most patients with severe congestive failure, which persists despite extensive medical therapy, are unlikely to be helped by operation and usually fail to survive it. Occasionally, however, such patients are improved. It is, therefore, difficult in an otherwise hopeless situation to deny a patient whatever small chance operation offers.

4. The presence of a loud apical systolic murmur suggests the possibility of predominant mitral insufficiency, but does not guarantee its presence. Often, despite this auscultatory finding, the patient proves to have severe stenosis and derives a great benefit from simple commissurotomy. Various workers are attempting to develop methods for correcting severe mitral insufficiency, but at present these must be considered experimental. Most cardiologists strive to exclude from operation those patients whose lesion is predominantly mitral incompetence. This has been difficult to do by the ordinary methods of physical examination and standard roentgenographic studies. Various techniques have been tested in an attempt to determine whether or not mitral stenosis predominates. In our hands, angiocardiography has been most helpful in assessing the relative severity of stenosis and insufficiency.[5] A characteristic pattern of opacification has been recognized for pure mitral stenosis of a severe degree, and a different angiocardiographic pattern has been found in the presence of a "wide-open" valvular insufficiency. In pure mitral stenosis the left atrium remains sharply outlined and densely opacified for a long period, whereas the left ventricle is poorly opacified and small. In severe mitral incompetence, the left atrium and left ventricle are equally opacified and the left ventricle is enlarged. Such findings help to decide the significance of the apical systolic murmurs in many instances. Unfortunately, the angiocardiographic pattern occasionally lies somewhere between the two extremes, and a decision may be difficult.

At operation, the finding of a regurgitant jet does not necessarily indicate that the result of commissurotomy will prove unsatisfactory. The relative size of the mitral opening, and not the actual size, is the important factor. Thus, in several patients with strong regurgitant jets, when the actual size of the opening was not small, great improvement has resulted from further increasing the opening, making it correspond more closely to the size of the enlarged heart. Had we used one of the procedures for correction of mitral insufficiency, we would have credited it with the good result, whereas simple commissurotomy was the only procedure employed.

5. Disease of other valves complicating mitral stenosis was formerly considered an absolute contraindication to operation. At present, when aortic

stenosis complicates mitral stenosis, it may be dealt with surgically at the same time. Its preoperative recognition may be difficult, since severe mitral obstruction reduces the intensity of the aortic murmur. One of our patients early in the mitral series died because no significant aortic systolic murmur could be heard until postoperatively, after the mitral valve had been opened. This is no longer a problem since we have adopted routine palpation of the aorta after mitral commissurotomy to determine the presence of a systolic thrill.

Aortic insufficiency is a more difficult problem. Patients with mitral stenosis and mild degrees of aortic incompetence usually benefit from mitral commissurotomy. If the aortic regurgitation is of a degree sufficient to cause a widened pulse pressure it seems likely that the patient would require something more than commissurotomy in order to expect much improvement. In many patients, the basal diastolic murmur has evidently been of pulmonic rather than aortic origin and has disappeared following mitral commissurotomy.

6. Pregnancy is not an absolute contraindication to operation. Since, with good medical management, most mitral patients withstand pregnancy fairly well, elective valvulotomy can usually be postponed until after delivery. In patients showing evidence of failure before the seventh month we have occasionally recommended valvulotomy, however, especially when the termination of pregnancy was not desirable.

7. It has been suggested that the vascular changes which occur in the lungs secondary to mitral stenosis may be irreversible.[6] It has been feared therefore that, when severe, a vascular block might remain in the lungs even after relief from mitral stenosis. We do not believe that a patient should be refused the benefit of surgery on such a basis. Our experience suggests that if a patient can be carried through the operation and if the mitral block is released, improvement will usually result.

8. Patients with mitral stenosis and minimal or no symptoms require special consideration. Formerly, most cardiologists refused to refer such patients for operation. However, the operation has reached a stage in its development which permits offering it to patients with hope of considerable benefit and with relatively low risk. If a patient has signs that mitral stenosis is causing left atrial enlargement and pulmonary congestion, it is difficult to see the advantage of waiting until auricular fibrillation, embolization, cardiac enlargement, and congestive failure develop.

Preoperative Preparation.—An important objective in the preparation for operation is to have the patient free of excess fluid. Even a patient who appears to have no cardiac failure often loses a few pounds following administration of a mercurial diuretic. The good-risk patient will need little in the way of preparation, but the patient in severe failure may require several weeks, and in fact may never be successfully prepared. All of the usual medical means of getting patients out of heart failure may be employed. In the great majority of patients, the judicious use of digitalis and mercurial diuretics will be adequate. At times the use of resins has apparently been helpful.

Anesthesia.—The most important objectives in the anesthetization of the patient for cardiac surgery are to keep the patient light and well oxygenated. The choice of anesthetic agents is probably not a matter of great importance. Until an anesthetist has had experience in this field he is likely to carry the patient in too deep a plane of anesthesia and may not realize how vigorous the ventilation needs to be to maintain maximal oxygenation of the myocardium.

Operative Technique.—The lateral approach offers many advantages to the surgeon, especially if technical difficulties are encountered. The left fourth intercostal space is opened almost in its entirety. The patient may be rotated backward slightly and the lung held posteriorly as the pericardium is opened behind the phrenic nerve. A purse-string suture is placed around the auricular appendage and is attached to a Rumel tourniquet. An anesthetist prepares to occlude the carotid arteries in the neck, or tourniquets are placed around them in the superior mediastinum. The carotids are occluded momentarily whenever the auricle is manipulated. It is probably not wise to occlude them for more than twenty to thirty seconds at a time.

The auricular appendage is cut open and allowed to bleed before the clamp is applied, in the hope that blood clots, if present, may escape. Traction sutures are placed on the edge of the auricular appendage, and the opening is enlarged enough to accommodate the finger. More blood is allowed to escape in the hope of evacuating clots. The right index finger is inserted as the auricular clamp is released, and the mitral valve is carefully palpated. After determining the characteristics of the valve and estimating the degree of regurgitation, if any, finger fracture is attempted. Some surgeons state that finger fracture is almost uniformly successful, whereas others believe that the use of a knife is almost always necessary. We have preferred to use finger fracture but have found that the use of a knife was necessary in about one-third of the patients. It has been our impression that regurgitation is less likely when the valve is opened by finger fracture than when it is opened with a knife. The guillotine-type knife has been used primarily in this series. We feel that the ideal knife is not yet available.

When opening the mitral valve, the surgeon is constantly faced with the problem of when to stop. We believe that we have probably stopped too soon on some occasions and not soon enough in others. We now believe that the surgeon should persist until the anterolateral commissure is opened entirely out to the myocardium. The surgeon should not be content to leave a little rim, for when that final bit is cut it may add greatly to the opening obtained.

We have been more cautious with the posteromedial commissure. When it can be opened by finger fracture, we do so, but if the anterolateral commissure is opened widely we are hesitant to use a knife on the posteromedial commissure. It is our impression that we have produced the most severe regurgitation when cutting this commissure.

The type of valve encountered may vary greatly. Ideally, the valve barely admits the index finger and is thin, but sufficiently rigid so that it can be torn in both commissures by finger fracture. At times a similar valve may be so

elastic that it cannot be torn by finger fracture. It may be pushed up against the heart wall without tearing. In such a situation we have had to use a knife.

The very thick, badly diseased valves vary also. Some may be so friable that they can easily be torn by finger fracture. More often, perhaps, a knife is needed to start the tear in the commissure, even though the finger may extend it out to the muscle. At times a rigid valve which cannot be fractured does not seem to open satisfactorily even when cut. In some instances, if the rigid portions of the valve can be cut entirely out into the myocardium, some separation of the rigid edges may result.

A most difficult problem is the large heart with regurgitation. The regurgitation is most often present in the posterior part of the opening. We have never felt justified in cutting the posterior commissure under these circumstances. There has been considerable improvement, however, when the anterior commissure was opened to reduce the stenosis in that area.

Some surgeons have stated that opening the commissures in the presence of a regurgitant valve may increase its efficiency and reduce regurgitation. If this has happened in our experience, we have not been aware of it.

In closing the auricular appendage, the finger is withdrawn and the clamp reapplied. The purse-string suture is then tied. This may be reinforced with a free ligature, if desired. Sutures are placed in the cuff to prevent any possible slipping.

Intra-Auricular Blood Clots.—Occasionally the auricle may be so filled with clots that no bleeding occurs when the incision is made into the appendage. Some surgeons have advocated going through one of the pulmonary veins, but the reported mortality rate of that procedure has been high. When the clot seems small, it may be possible to express it from the auricle. In many instances, however, it is large and firm, and the problem is whether to back out, to go through the clot, or to go around it. With the carotids occluded, we have cautiously worked the finger between the clot and the auricular wall sufficiently to enter the free auricular cavity and to get at the mitral valve. Even with the greatest care, an embolus is a grave risk under these circumstances. In our entire series, we have had five cerebral emboli at the time of operation. In two instances, when the patient awoke with a right hemiplegia, the left carotid pulse was not palpable. The patients were taken back to the operating room immediately. When the carotid artery was opened there was no flow from the proximal end. A suction tube was gently pushed down the carotid, and in both instances a normal blood flow was re-established. Whether the embolus was pulled through the suction tube, or was dislodged and landed in a silent area of the arterial tree, was never ascertained. In both instances the patients awoke without the hemiplegia.

Small Auricular Appendage.—The auricular appendage may be small or almost entirely obliterated. The problem then arises as to whether the auricle can be safely entered. Certainly the possibility of sudden catastrophic hemorrhage is terrifying. With experience and care, the probability of catastrophic

hemorrhage can be minimized, but probably never eliminated. We attempt to make the incision in the auricle in such a way that a clamp will cover it as the finger is withdrawn. This is usually, but not always, possible.

The greatest danger arises when the finger or knife tears the auricular wall beyond the line of incision and especially beyond the purse-string suture. When this occurs, it is probably a mistake to remove the finger and attempt to tie the purse-string suture or to remove the finger and attempt to catch the edge of the auricle with a clamp. If the finger is removed and the clamp cannot be applied to occlude the torn area, there will be massive hemorrhage. Perhaps the best maneuver is to keep the finger in the auricle. The purse-string suture may be tightened around it, and pressure applied by the finger within the auricle may occlude the torn area. The tear may then be sutured or the entire opening in the auricle may be sutured as the finger is slowly withdrawn.

Postoperative Care.—Special attention should be given to the parenteral administration of fluids during the early postoperative period, as well as in the operating room. Overtransfusion is a hazard. We do not hesitate to replace the blood loss, however, if the blood pressure is not maintained postoperatively.

Mercurial diuretics have been useful during the postoperative period, especially when the patient was a poor risk or the valve was not satisfactorily opened. When the valve has been opened widely, the postoperative course is usually no great problem.

Oxygen therapy appears to be helpful for a day or so. It is, of course, important to keep the tracheobronchial tree clear. If too much difficulty is encountered with this, a tracheotomy is advisable. Tracheotomy should always be performed in patients with hemiplegia.

The low-salt syndrome may result from preoperative efforts to rid the body of excessive fluid. Apparently this becomes a problem, however, only in the very poor-risk patient. When the sodium does become depleted by this mechanism, its return toward normal by additional therapy is likely to add water to the body as well. If the heart failure is sufficiently bad, it may be impossible to maintain chemical balance and at the same time keep the patient free of fluid. In the average patient this problem can be avoided by relaxing the diet once the mitral stenosis has been released.

Pericardial Effusion.—In spite of leaving a large opening in the pericardial sac at the time of operation, this opening is likely to seal over, and an effusion may develop in some patients. A good many of the hearts appear to be increased in size postoperatively. How often this is due to pericardial effusion is not known. It is suspected when there is cardiac enlargement or a continuing low-grade fever, or when the patient is not doing as well as had been anticipated. We found it necessary to tap the pericardium postoperatively only once in this series, however.

Thrombosis and Embolism.—Postoperative pulmonary emboli have been fairly common in this series but did not appear to be the major cause of death in any case. In addition to the five major cerebral emboli at or immediately after operation, there have been three postoperative emboli. One lodged in the popliteal artery and was successfully removed, and in the others, there

were small cerebral emboli at autopsy. Whether they were the cause of death is uncertain. Three other patients had mild cerebral symptoms which suggested that there may have been small emboli. They were in chemical balance. Two instances of fatal embolism occurred after discharge from the hospital.

In our effort to minimize postoperative clotting on the valve or auricle, we have used heparin postoperatively when the patient had previously had an embolus, when there was a palpable clot in the auricle, when there was a ragged tear on the valve, and when there was a ragged tear into the myocardium. If a clot was obviously left behind in the auricle, anticoagulant therapy was continued for several months.

Results.—One hundred forty patients have been operated upon with thirteen hospital deaths. Of the first twenty-five patients operated upon, six died in the hospital and four have since died of their disease. One additional patient who got an excellent result died two years later of leukemia.

In the next 100 patients, whose follow-up period has been long enough to evaluate the results, there were six hospital deaths. One was a very poor-risk patient with a calcified auricular wall, and we were unable to enter the auricle. One had a catastrophic hemorrhage from inadvertently tearing the greatly distended pulmonary artery. One man, aged 57, died of an acute coronary occlusion. Two Grade 4 patients had multiple small cerebral emboli at autopsy, but whether they were the primary cause of death is uncertain. One patient with hypertension apparently died of heart failure. There were three delayed deaths. Two of these were due to our failure to improve the valve sufficiently; the other was sudden and unexpected in a patient with hypertension.

Of the ninety-one patients who remain alive, forty-three have had excellent results, forty-two have had moderately good results, and six have been improved little, if at all.

AORTIC STENOSIS

An operation for aortic stenosis developed more slowly than that for mitral stenosis. Smithy[7] had some success in using a cutting instrument, but there was always the fear of producing fatal regurgitation. It was natural to suppose that the commissures of the aortic valve should respond to a tearing force in the same manner as the mitral commissures do to finger fracture. Efforts at finger fracture, however, proved catastrophic. The problems to be solved were (1) how to approach the valve, (2) how to produce an instrument strong enough to open the fused aortic commissures, and (3) how to get such an instrument through the stenotic aortic valve. These problems have not been entirely solved, but the Bailey aortic dilator[8] is a good start. It is designed to go through the left ventricle. It threads a beaded wire through the stenotic valve and thereby minimizes the risk of creating a false passage. The instrument up to now has not been quite strong enough, for we have broken the head twice in attempting to open valves, but efforts are being made to strengthen it.

Selection of Patients.—The patient with an isolated aortic stenosis does not go into right-sided heart failure until fairly late in the course of the disease.

It is felt, therefore, that when such a patient becomes incapacitated by anginal pain or by dyspnea on slight exertion he should be operated upon.

When aortic stenosis coexists with mitral stenosis, it should be corrected at the same time. The aorta should be palpated at each operation for mitral stenosis. If the thrill of a jet of blood coming through a stenotic valve is palpable, the valve should certainly be dilated. When there is only a slight thrill, indicating some minimal disease of the aortic valve, it may be difficult to know whether or not to dilate it. One of our patients with mitral stenosis who died of an acute coronary occlusion had a slight aortic thrill at operation but was not dilated. At autopsy he had a slight stenosis but probably not one of significance.

The patient who has aortic stenosis and regurgitation presents a problem, When the stenosis is the predominant lesion, he should have the valve dilated. When the regurgitation is the predominant lesion, something more than aortic dilatation is obviously required.

Operative Technique.—We have opened almost the entire left fifth intercostal space with the patient in the lateral position. When there is both aortic and mitral stenosis, the mitral commissurotomy is performed first. Even when no mitral disease is suspected, we have usually palpated the mitral valve to exclude a hidden stenosis.

The greatest fear in the attack on the aortic valve is that of ventricular fibrillation as the result of traversing the left ventricular wall. The incidence has been sufficiently great to cause Bailey to experiment again with attacking the valve through the aorta. We believe that the greatest protection against ventricular fibrillation is hyperventilation of the lungs until the left ventricular wall is pink. This must be done before starting to work on the ventricular wall. We also believe that procaine injected locally is helpful.

The selection of the site to enter the left ventricle is important. Care should be taken to avoid injury to any visible vessels. It is thought best not to go too close to the apex where the myocardium is thin. As a rule, a site may be found relatively free of vessels, fairly close to the septum (to avoid getting involved in the chordae tendineae), and about halfway between the base and the apex of the heart, or perhaps a little closer to the apex.

The pressures in the left ventricle may be very high, and consequently there is always fear of catastrophic hemorrhage during this procedure. If proper precautions are taken this should not be too great a problem. The most important thing is to have a clean incision in the ventricular wall. If a stellate fracture of the wall is produced, hemostasis may be difficult or impossible to secure.

A triangular suture is placed in the myocardium first. There should be 1 cm. or more between the points of entry and exit of the suture to allow a broad area of epicardium to be involved, since it is stronger than the myocardium itself. A Rumel tourniquet may then be applied to the triangular suture.

A small incision is first made in the ventricular wall and the beaded wire is inserted. If it passes through the aortic valve, it may be felt in the aorta

between the fingers of the left hand. The incision in the ventricular wall is then extended sufficiently to admit the head of the dilating instrument without tearing. The instrument is passed over the wire and can be felt to go through the valve and into the aorta. There may be considerable resistance to the passage of the instrument through the valve if the stenosis is severe. The head can be felt to be in place, with the left hand compressing the aorta. The handles of the instrument are then closed, opening the dilating head and tearing open the valve. There may be considerable resistance. The head can then be closed and the instrument removed.

The person holding the tourniquet on the triangular suture should not be too enthusiastic in its use. If this suture were to tear through the myocardium, recovery would be difficult or impossible. We have preferred to accept a bit of bleeding around the instrument rather than risk a catastrophe, and so have applied light pressure, if any, on the tourniquet. Once the instrument is out and a sponge is held over the incision for awhile, the bleeding will decrease rapidly, and it may then be completely controlled by a few mattress sutures.

In the two instances in which the dilating head broke while in the valve, it could not be closed entirely to be brought out of the heart. Fortunately, in its delivery, a catastrophic tear of the ventricular wall did not occur.

The problem of dealing with ventricular fibrillation, when it occurs in the presence of large hearts, is a difficult one. It is difficult to establish a good blood flow by cardiac compression because of the thick wall and the small chamber. It is, therefore, difficult to obtain maximum oxygenation of the myocardium before the electric shock is applied. Moreover, such a large heart is not readily defibrillated without using currents which may burn the heart. This problem is most troublesome in the patients with pure aortic stenosis, since the patients with coexisting mitral stenosis do not have such large left ventricles.

Results.—Ten patients have been operated upon. Three of these had no mitral disease, while seven also had mitral stenosis. There was one death due to ventricular fibrillation as the valve was being opened in a patient with aortic stenosis and a large left ventricle. Of the others, seven have been improved. Two are too recent to evaluate, but improvement is anticipated. In some it has been difficult to know whether the mitral or aortic valvulotomy accounted for the improvement. In others the mitral valve was diseased only slightly or not at all so that the improvement can be attributed solely to the aortic manipulation. The nine cases may be grouped as follows: four greatly improved, two moderately improved, and one slightly improved. Two were operated upon too recently to evaluate.

The postoperative systolic blood pressures have been higher in all instances. In no instance have we been sure that aortic regurgitation was increased. In one patient the diastolic aortic murmur is definitely louder, but the patient is so greatly improved that we have preferred to believe that

this is due to the increased blood flow incident to the mitral commissurotomy. The unchanged postoperative diastolic blood pressures have supported that belief.

Autopsy on the patient who died showed one commissure torn open entirely out to the wall, one torn half-way, and the third not at all. It was perfectly obvious, however, that if the patient had survived he would have been greatly improved.

SUMMARY

1. The problems of selection of patients for surgery on the mitral and aortic valves have been discussed.

2. Angiocardiography has proved to be a useful technique in selecting patients with mitral stenosis.

3. We have used a knife in approximately one-third of the mitral valves operated upon in this series.

4. Of the last 100 patients with mitral stenosis operated upon in this series, there were six operative deaths and three delayed deaths. Of the remainder, forty-three have excellent improvement, forty-two have moderate improvement, and six have improved little, if at all.

5. Of ten patients subjected to dilatation of the aortic valve, one died, four were greatly improved, two moderately improved, one slightly improved, and two were treated too recently to evaluate.

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EXPERIMENTAL SURGICAL REPAIR OF VENTRICULAR SEPTAL DEFECTS

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DEFECTS of the ventricular septum occurring alone, or in combination with other anomalies, constitute one of the commonest congenital malformations of the heart. Although the clinical course of patients with isolated interventricular defects is not as well known as would be desirable, it is obvious that this abnormality is poorly tolerated by numerous individuals and that it may lead to cadiac invalidism and premature death. Up to the present time only a few experimental and clinical observations concerning the closure of such defects are available in the literature. It is our purpose to describe a method which has proved successful.

EXPERIMENTAL METHOD

Healthy mongrel dogs were used. Large interventricular defects were created by a method which has been described elsewhere.[1] The defects were usually made some weeks or months before closure was attempted, although occasionally they were produced immediately before repair. The animals were anesthetized with an ether-oxygen mixture administered intratracheally by means of an intermittent positive pressure apparatus following induction with pentobarbital sodium. All procedures were carried out under rigidly aseptic conditions. The ventricular portion of the heart was exposed through a right fifth intercostal space thoracotomy and wide longitudinal incision of the pericardium. Traction sutures were placed in the right ventricular myocardium, and an incision in line with the cardiac muscle fibers was made extending partially through the heart wall. The left index finger was placed over this incision, and the blades of a curved scissors were introduced under the finger into the incision. By spreading the blades, the wound was extended into the ventricular cavity and made of adequate size. Compression with the overlying finger permitted the accomplishment of this procedure with minimal loss of blood. The finger was then quickly passed into the ventricular chamber. The defect itself could usually be located with relative ease, and a strong jet of blood was palpable in the area of the shunt.

Once the defect was located, the finger was swung along the septum toward the left border of the heart and, using the finger as a guide, a large

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round blunt-tipped needle (Fig. 1) was passed through the ventricular wall just anterior to the coronary vessels and directly into the septum itself. With the guidance of the finger in the ventricle it was possible to keep the needle within the septum and to direct it toward the mid-portion of the defect. The needle was then passed into the opposite wall of the defect, through the remaining portion of the septum, and out of the heart wall. Attached to the needle was a previously formed distensible tube constructed of autogenous pericardium or of thinly woven nylon. Through the other end of the tube from that fixed to the needle, a plastic catheter had been ligated in place so that one end of it opened into the central portion of the tube. With little difficulty the distensible tube could be drawn through the septum in the path of the needle, and the palpating finger could feel its mid-portion presenting in the region of the defect. Once the tube was properly placed, blood was withdrawn from the ventricle into a syringe containing approximately 1 c.c. of penicillin solution. The blood was then injected through the polyethylene catheter until the tube could be felt bulging out snugly in the defect and completely obstructing it (Fig. 2). Since closure was associated with abolition of the cardiac thrill, the finger was often withdrawn from the ventricular cavity and the ventriculotomy was closed with interrupted silk sutures before the tube was distended with blood. Once the operator was satisfied that the tube had been sufficiently distended to close the defect and that enough time had passed to permit clotting of the injected blood, the plastic catheter was withdrawn as the protruding portion of the graft was securely ligated. Both ends of the graft were then sutured to the myocardium at the points of emergence. The pericardium was loosely approximated with silk sutures, unless it had been excised for construction of the graft, and the chest wall was repaired with interrupted sutures to the various layers after expanding the lungs fully.

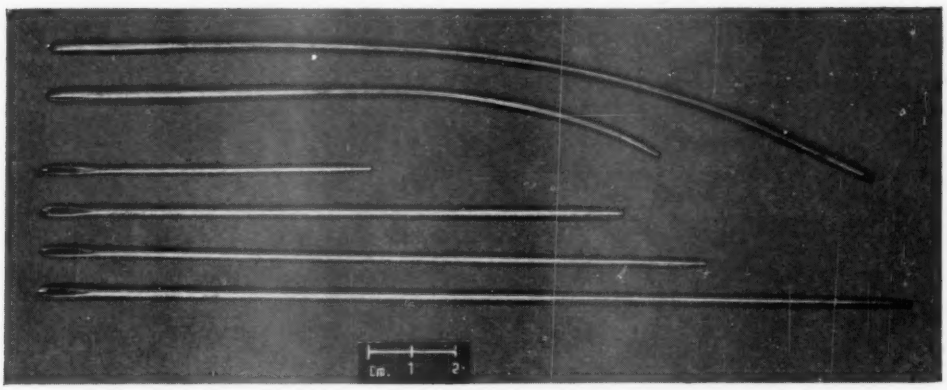

Fig. 1.—Photograph of straight and curved large blunt-tipped needles used in repair of ventricular septal defects.

The pericardial tubes were made in the following manner: a rectangular portion of pericardium about 4 cm. wide and as long as possible was excised and, after trimming away from the external surface any attached fatty tissue, the strip was folded on itself with the smooth cardiac side of the pericardium

within. The approximated edges of the middle 3 or 4 cm. were tightly closed with a continuous suture of 00000 Deknatel. After making sure that this portion of the tube was watertight, we turned the tube inside out. One end of the sutured portion of the tube was transfixed with silk, and the strip of pericardium beyond it was trimmed and threaded onto a long needle. The other end of the sutured portion of the tube was snugly ligated about a small

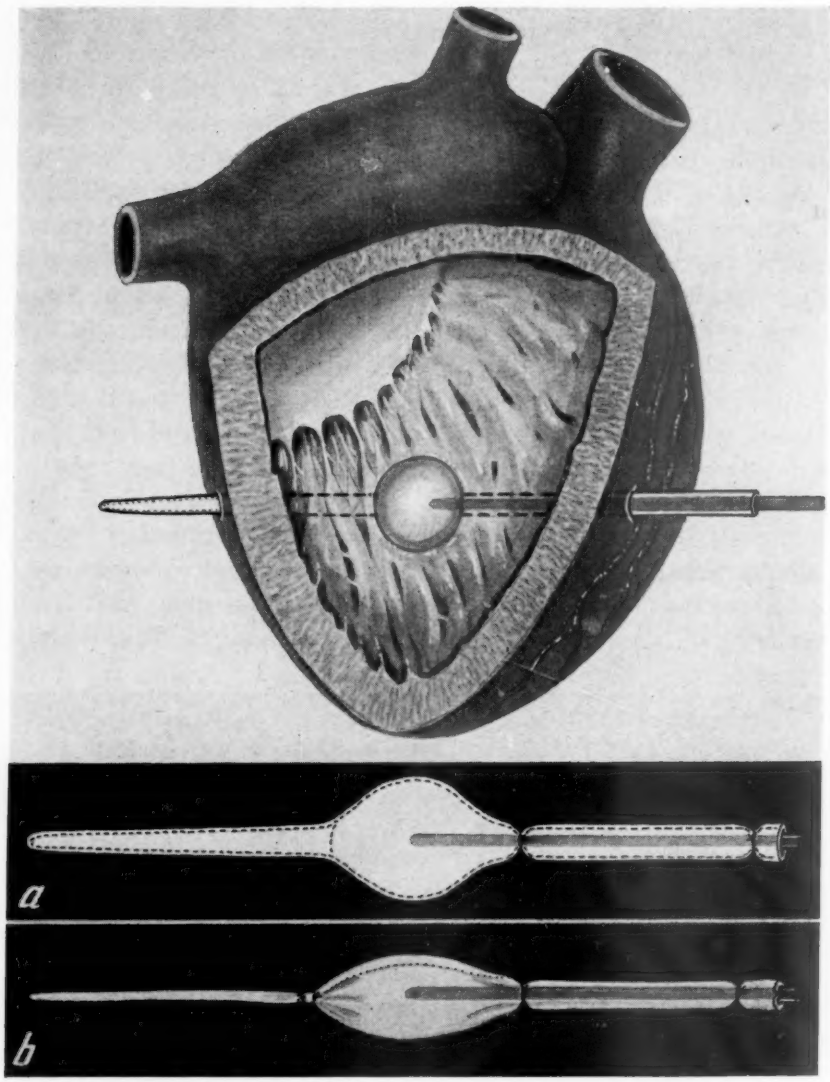

Fig. 2.—Schematic diagram of distensible tube which has been drawn through the center of the defect and inflated with blood. Below are illustrated tubes constructed of nylon and of pericardium.

plastic catheter, the tip of which lay in the mid-portion of the tube. Care was taken to keep the cardiac surface of the pericardium moist and to avoid injury to it.

The nylon tubes were constructed of lightweight nylon cloth which has a thread count of 176 lengthwise and 118 in the other direction. The cloth was folded on itself and the graft was fashioned by sewing together the two layers with fine nylon thread using an ordinary sewing machine. The mid-portion of the graft was elliptical or round in shape and approximately 3.5 cm. in width at its widest portion. It was closed at one end, and from this end extended a ribbon about 6 to 8 cm. long and 3 to 4 mm. wide. This end was threaded onto a needle. The other end of the graft was similar in size, but was left as a tube communicating with the central portion of the graft. A small plastic catheter was passed through it into the mid-portion of the potential balloon and was securely ligated in place. Before being passed into the septum it was autoclaved and soaked in sterile mineral oil or thoroughly greased with sterile petroleum jelly. The latter method seemed more effective in rendering it impervious to blood.

When pericardial grafts were used, the tube was easily distended with blood and readily occluded the defect. It was allowed to bulge equally beyond the right and left sides of the septal wall. When blood was first injected into the nylon tubes, leakage sometimes occurred, and subsequent injections were usually necessary before proper distention was achieved. Generally, closure of the defect by a nylon sac was easier to accomplish when the sac was pushed slightly into the left ventricle by the intracardiac finger before it was distended.

EXPERIMENTAL OBSERVATIONS

A pericardial sac was utilized for operative closure in thirteen animals (Table I). Four animals were operated upon before the present technique was perfected. In three instances, a simple pericardial balloon about 1½ cm. in diameter and about 2 cm. long, with a plaster catheter attached at one end and a silk suture at the other, was used. In the fourth case, the tube was constructed in a similar fashion to that previously described but was too small in diameter. Complete closure of the ventricular defect was obtained in one animal, and the closure was incomplete in the other three animals. Only a 1 to 2 mm. defect remained in two animals, while the defect of the third was only about three-quarters closed.

Nine animals were operated upon after the development of the present technique. One dog died at the time of operation. The defect in this animal was located immediately beneath the pulmonary valve in the pulmonary outflow tract. The proximal portion of the tube was misplaced and lay within the infundibular portion of the right ventricle and not within the septum. Expansion of the sac, therefore, caused obstruction of the blood flow to the lungs, and ventricular fibrillation resulted. Five animals were sacrificed from 29 to 106 days after operation, and the septal defect was found to be completely closed in all of them. Three animals have been kept for longer observation. At the present time they have been alive and well from 84 to 120 days following operation. No thrill or murmur has been present since the time of operative repair, and it is presumed that complete closure has been obtained in all.

TABLE I. RESULTS OF CLOSURE OF VENTRICULAR SEPTAL DEFECTS WITH PERICARDIAL TUBES

DOG	INTERVAL BETWEEN CREATION AND CLOSURE OF DEFECT (DAYS)	OBVIOUS HEART FAILURE AT TIME OF OPERATION	COMPLETENESS OF CLOSURE		INTERVAL BETWEEN CLOSURE AND POST-MORTEM EXAMINATION (DAYS)	REMARKS
			POST-MORTEM EXAMINATION	CLINICAL CLOSURE BY ABSENCE OF THRILL AND MURMUR		
			Preliminary Operations			
1	20	+	1 to 2 mm. defect		5	
2	21	+	Complete		61	
3	30	+	About ¾ closed		15	Poor placement of graft
4	11	+	1 to 2 mm.		Few hours	Sac too small
			Observations With Final Method			
5	51	0	Complete		52	
6	12	+	Complete		106	
7	21	0	Complete		94	
8	11	0		+		Alive 120 days postoperative
9	7	+		+		Alive 103 days postoperative
10	14	±	Complete		29	
11	0	0	Complete		84	
12	0	0		+		Alive 82 days postoperative
13	8	+	Partial			High defect; graft poorly placed with obstruction of pulmonary artery

Nylon tubes have been utilized for closure of ventricular septal defects in twenty animals (Table II). In the beginning the results were poor because the expansible portion of the tube was made too small. These small sacs were used in four animals (Dogs 1, 2, 3, and 4), and incomplete closure of the septal defect resulted in all. Two animals (Dogs 2 and 3) are alive sixty-one to sixty-six days after operation, and both are in moderate heart failure and demonstrate a loud systolic thrill and murmur. Two animals were sacrificed. The defect was only about half-closed in one, and in the other a tiny 1 to 2 mm. defect remained.

A larger nylon tube was used in sixteen animals. In fourteen of them the sac was soaked in mineral oil before repair, and in 2 a thin layer of petroleum jelly was applied to the nylon. The hearts of eight dogs were examined after operative repair, and the septal defect was found to be completely closed in three. Small communications 1 to 3 mm. in diameter persisted in four dogs, while in one the sac had deflated and a defect of almost original size remained. Eight animals are alive. In six of them the systolic thrill and murmur completely disappeared following operative repair, and it is presumed that their defects are completely closed. In one animal a systolic thrill recurred a few hours after operation and a large communication is undoubtedly still present. Another dog had persistence of a systolic murmur over the right chest, but the systolic thrill disappeared. These physical signs indicate that the defect

is almost completely closed. In seven animals (Dogs 13, 14, 15, 16, 17, 18, and 19) the sac was pushed slightly into the left ventricle before it was expanded; five had complete closure and one almost-complete closure, and in only one was a poor closure obtained.

TABLE II. PRELIMINARY OBSERVATIONS ON CLOSURE OF VENTRICULAR SEPTAL DEFECTS WITH NYLON TUBES

DOG	INTERVAL BETWEEN CREATION AND CLOSURE OF DEFECT (DAYS)	COMPLETENESS OF CLOSURE: POST-MORTEM EXAMINATION	COMPLETENESS OF CLOSURE: CLINICAL CLOSURE BY ABSENCE OF THRILL AND MURMUR	INTERVAL BETWEEN CLOSURE AND POST-MORTEM EXAMINATION (DAYS)	REMARKS
1	0	1 to 2 mm.		13	
2	0		Thrill persists		Alive 66 days post-operative
3	0		Thrill persists		Alive 61 days post-operative
4	0	Half-closed		2	Sac leaked
5	0		+		Alive 57 days post-operative
6	27		+		Alive 57 days post-operative
7	66	3 mm.		40	In failure at time of repair; thrill gone after repair
8	25	Complete		11	
9	0	1 mm.		36	
10	0	2 mm.		2	
11	0	Complete		28	
12	0	3 mm.		1	
13	0		+		Alive 38 days post-operative
14	0		Thrill persists		Alive 38 days post-operative
15	31	Complete		19	
16	0		+		Alive 33 days post-operative
17	0		+		Alive 26 days post-operative; massive ascites at time of repair; ascites disappeared after closure
18	106		Thrill gone Murmur persists		Alive 26 days post-operative
19	0		+		Alive 19 days post-operative
20	0	Half-closed		2	Sac leaked

It was obvious that the principal difficulty with the use of nylon grafts resulted from the leakage of blood from the distended sac. Almost invariably the initial injection of blood closed the defect so that the thrill disappeared. Usually, however, a faint thrill reappeared shortly afterward and would disappear with a subsequent injection of blood. In many cases the resulting thrombus within the tube was of sufficient size to result in permanent complete closure of the defect. On the other hand, it was apparent that most of the failures resulted from further loss of blood from the graft.

In a few animals, operative repair has been carried out with the use of expansible tubes constructed of different materials. In two dogs a sac was made by using a segment of autogenous vein. The vein was inverted so that the endothelial surface was external. Complete closure was not achieved in either case because the veins were too small in diameter, although at the time of post-mortem examination the vein grafts were found to have healed well with the wall of the defect. Crudely constructed tubes made of thin polyethylene sheeting were used in three dogs. In every case the thrill ceased

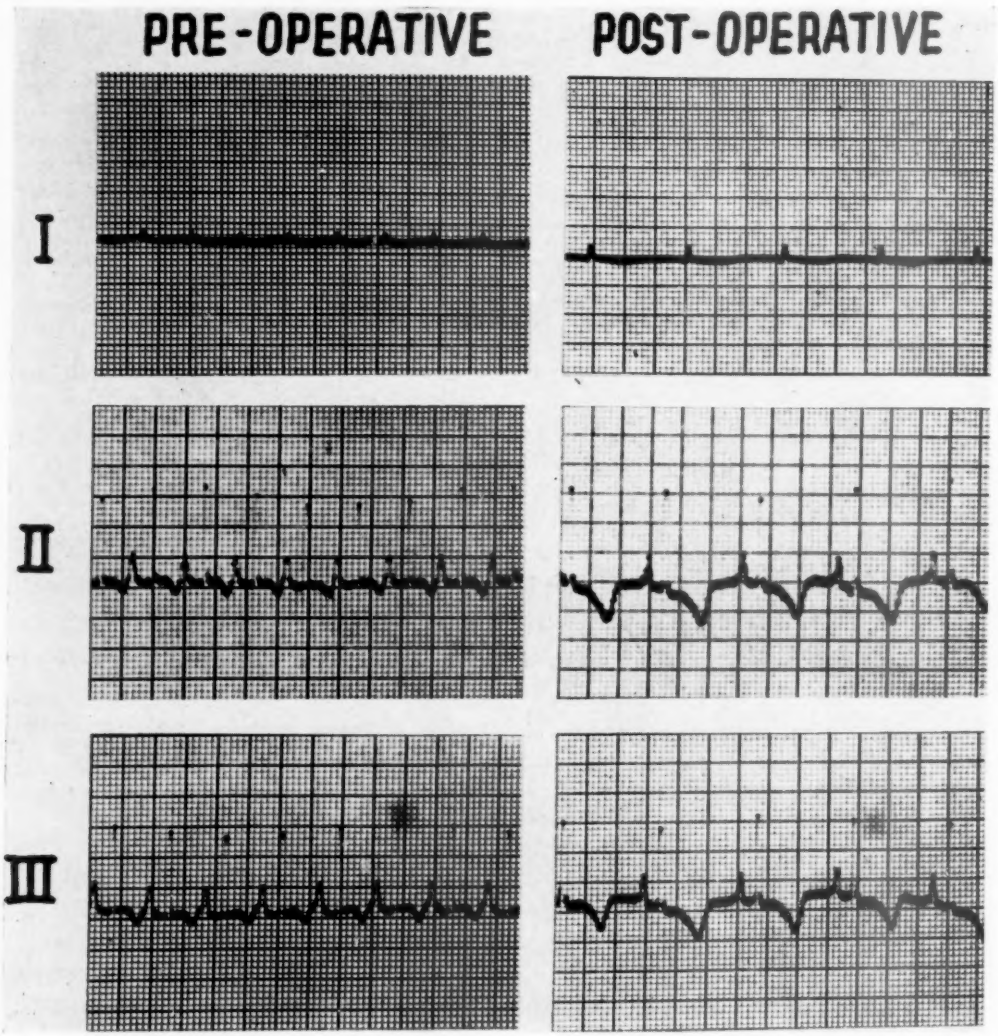

Fig. 3.—Leads I, II, and III of electrocardiograms made before and after operative repair of ventricular septal defect demonstrating the slowing of heart rate that often occurred and the absence of significant electrocardiographic alterations.

after the introduction of a few cubic centimeters of fluid into the sacs. However, the final results were poor because the tubes eventually developed leaks along the line of fusion of the polyethylene sac. The tubes then collapsed, and the ventricular communications recurred. An ordinary condom was drawn

through the defect in two animals. In both, the thrill disappeared after the introduction of from 2 to 4 c.c. of saline solution. Both are now alive and without systolic thrill or murmur two and three weeks, respectively, after operation.

At the time of operative repair some interesting observations were made. If an animal was in cardiac failure, the heart was usually markedly dilated and the rate rapid. The lungs often looked edematous and red. The slightest tear into the lung parenchyma produced a profuse hemorrhage. In some cases 200 or 300 c.c. of pleural fluid was encountered. Immediately after repair, the heart rate usually slowed (Fig. 3). After ten or fifteen minutes, the heart became smaller in size, and in some cases this change was dramatic. The edema of the lungs did not disappear so rapidly, although the color usually changed to a normal pink.

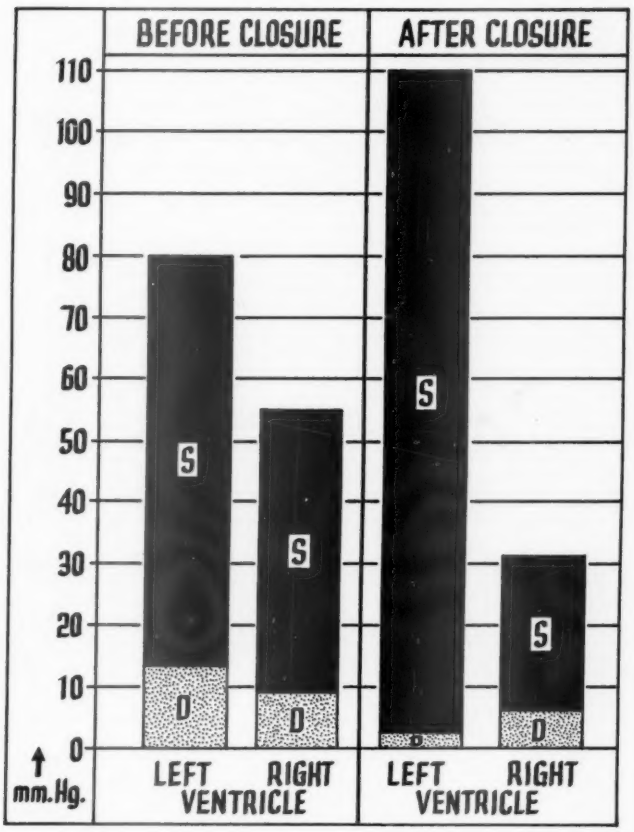

Fig. 4.—Diagram of left and right ventricular pressures before and after repair of a defect showing a decrease in right and an increase in left ventricular pressure after closure.

In a few animals, right and left ventricular pressures were recorded before and after closure. Before repair the right ventricular pressure was usually elevated and the left decreased as compared with normal values. Immediately after closure, the right ventricular pressure fell to normal and that of the left increased (Fig. 4). Electrocardiograms were made before and after operative

repair on many of the animals. A slight depression or elevation of the T wave was occasionally seen, but no significant abnormalities were encountered (Fig. 3). One severely ill animal demonstrated many ventricular extrasystoles just before operative repair. As soon as the defect was closed the arrythmia disappeared.

The animals were carefully followed after operation. Comparison of the clinical signs and post-mortem findings established the fact that the absence of a thrill and murmur signified complete closure of the communication. In those animals which demonstrated disappearance of the thrill, but persistence of a systolic murmur of less intensity, a small communication from 1 to 3 mm. in diameter was found at autopsy. The disappearance of the systolic thrill was a significant finding and always was associated with almost complete closure of the defect. If the thrill persisted after operation, the defect was invariably found to be poorly closed.

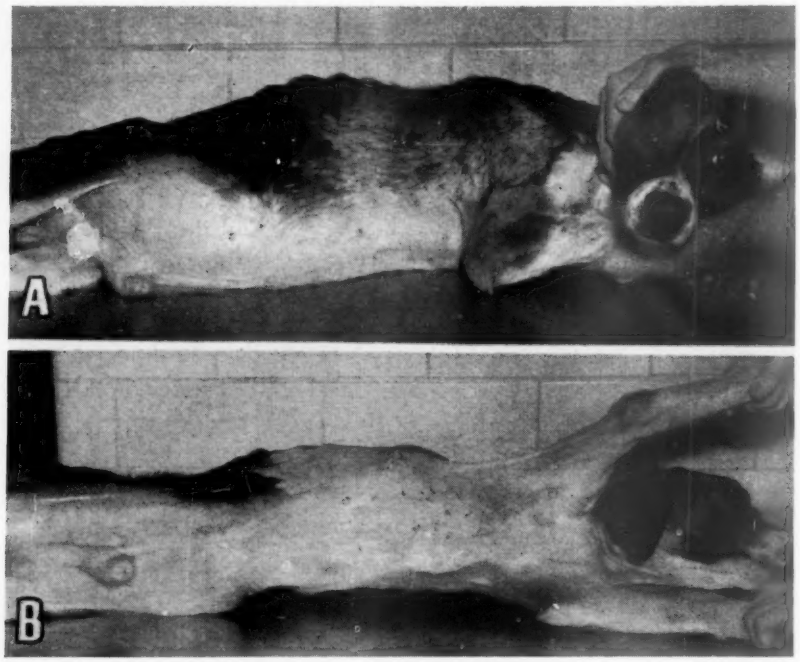

Fig. 5.—Photographs showing animal with massive ascites before, and the disappearance of the ascites after, repair of septal defect.

If the operative repair of the defect was complete or if only a small communication 1 to 3 mm. in diameter persisted, the animal's clinical course following operation was usually excellent. If he had been anorexic, lethargic, and malnourished as a result of heart failure and pulmonary congestion, his appetite and general condition improved remarkably shortly afterward. One animal developed right-sided heart failure about three weeks after its ventricular septal defect had been produced. At the time of operative repair three and one-half months after the first operation, he had massive ascites and was extremely ill. After the second procedure, in which a nylon tube was

used, the thrill disappeared, but a systolic murmur of low intensity could still be heard over the right chest. It was felt that these physical findings demonstrated that the defect was almost completely closed, and the subsequent clinical course substantiated this impression. During the next two weeks, the animal's general condition became much improved and the ascites gradually disappeared (Fig. 5). In spite of better eating, a weight loss of eight pounds within two weeks occurred. In one animal, cardiac catheterization was carried out before and after repair. Beforehand there was demonstrated a left-to-right shunt of 2.82 L. which represented 45 per cent of the left ventricular inflow. Afterward there was no evidence of shunt.

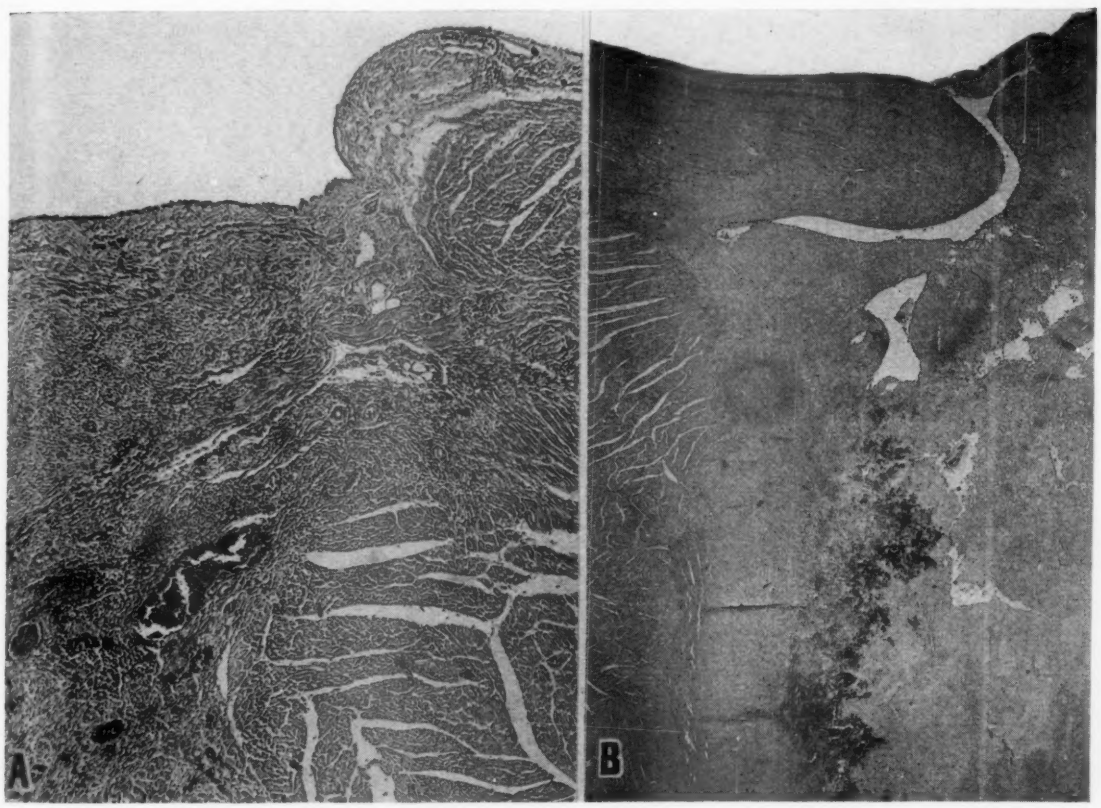

Fig. 6.—Photomicrograph of site of operative repair with a pericardial sac four weeks after operation showing (*A*) endothelialization of the graft from the edge of the defect and (*B*) the line of granulation and fibroplasia extending into the thrombus.

The site of operative repair was always carefully examined post mortem, and all but a few of the specimens were studied histologically. Shortly after repair, the pericardial grafts were smooth and free of clots. Endothelialization of the surface occurred rapidly, and by three or four weeks it was usually complete (Fig. 6, *A*). The grafts showed progressive organization of the thrombus and firm union with the margins of the defect (Figs. 6, 7, and 8). Microscopic studies revealed that at four weeks there was a line of granulation tissue and fibroblastic organization extending from the periphery into

the thrombus (Fig. 6). At the end of two months the thrombus was well organized except for a central core of granulation tissue (Fig. 8), and grossly at this time the grafts appeared smooth and well united with the septum (Fig. 9). Specimens studied three months after repair showed complete replacement of the thrombus with fibrous tissue. In general, the same process of fixation

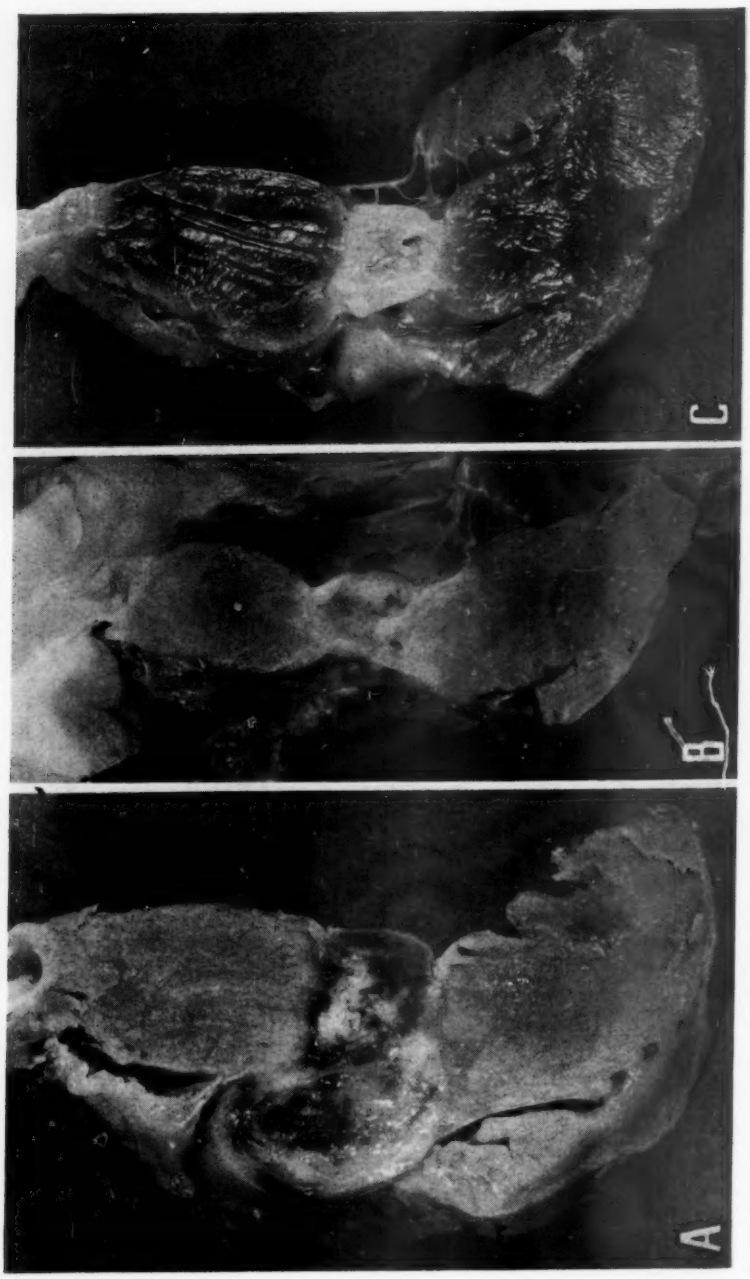

Fig. 7.—Photograph of vertical sections through ventricular septum and center of repaired defects approximately one month (*A*), two months (*B*), and three months (*C*) after operation, showing gradual contraction and organization of the pericardial graft.

of graft to septum, early endothelialization, and fibroblastic organization of the thrombus was observed when nylon grafts were used (Figs. 10 and 11).

DISCUSSION

In 1948, Murray[2] attempted to repair interventricular septal defects in three children by placing large sutures of fascia lata through the ventricular septum. A large skin or seamstress needle was passed into the septum using the eye as a blunt needle tip. The needle was directed into proper position by

Fig. 8.—Septal defect repaired two months previously with pericardial graft. *A*, Low-power photomicrograph through the center of the closed defect. *B*, High-power photomicrograph showing the surface of the endothelial lining of the graft and the organization of most of the thrombus with fibrous tissue.

utilizing the external anatomy of the heart and by palpation of the edges of the defect with the blunt end of the needle. All three patients withstood the operation well, and there was no evidence to suggest that the bundle of His had been injured. The immediate clinical results were encouraging, although one patient died one week after operation from atelectasis. The suture going through the heart was well placed and seemed to be in a position to occlude to a degree the patent interventricular septum.

Bailey and his associates[3] devised two methods for closure of interventricular defects. In one, a long rectangular pedicled pericardial graft was

drawn into the left ventricle through a single anterior puncture. The two leading corners of the graft were attached to sutures which emerged at different points in the posterior ventricular wall. The intracardiac portion of the graft was, therefore, stretched out over three points close to the interventricular septum and assumed a triangular outline similar to a diaper. This operation was performed on eleven animals. Sacrifice of the animals from four to ten weeks later showed the grafts to be atrophied, thickened, and shrunken with resultant deformity of the ventricular wall. It was obvious that these grafts could serve no useful function.

Fig. 9.—Photograph of left ventricular side of septum two months after operative repair showing pericardial graft completely obstructing defect and well healed to the septal margin.

A second technique was used in eighteen animals and three patients. A longitudinal incision was made approximately in the middle of the anterior aspect of the right ventricle. A curved probe threaded with heavy cotton suture was then passed through the right ventriculotomy and through the septal defect, and it emerged near the apex of the left ventricle. The end of the suture was grasped, and the probe was withdrawn from the heart. The free end of a previously prepared rectangular pedicled pericardial graft, rolled longitudinally into a solid tubelike structure somewhat over 1 cm. in diameter, was attached to the suture, which emerged through the right ven-

triculotomy. The tip of the graft was drawn into the right ventricle, through the defect, and out through the anterior left ventricular wall. Since large ventricular defects could not be produced without high mortality, the graft was simply forced through the intact septum in the experimental animal. Immediate fatality occurred due to hemorrhage in four of the eighteen dogs. One dog died from empyema, and the remaining thirteen animals were sacrificed at periods of from four weeks to one year following surgery. In each case, the grafts were healed and incorporated in the myocardium.

Three patients were operated upon by this technique. In one, the graft had to be withdrawn a few hours after its placement because obstruction of the pulmonary outflow tract had occurred. In another, the systolic thrill was completely abolished after operation, although a faint systolic murmur became audible eleven days later. In the third, a systolic murmur persisted after operation. In this case cardiac catheterization revealed a left-to-right shunt of 1.4 L. per minute before, and 1 L. per minute after, operation.

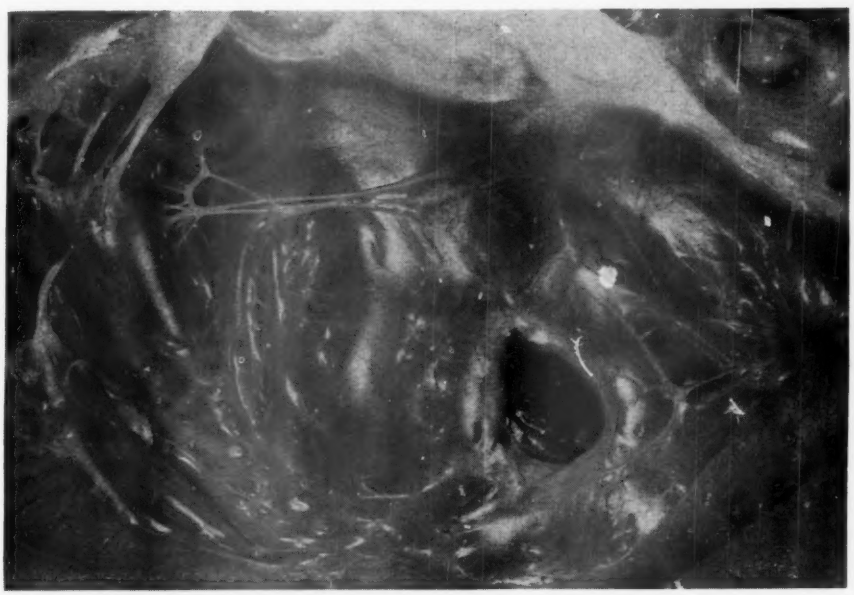

Fig. 10.—Photograph of left ventricular side of septum two weeks after operation showing closure of ventricular septal defect with nylon tube. Endothelialization has begun from the margins of the septum.

In the method which we have employed, a tubular graft is passed through the ventricular septum and the middle of the defect and is distended so that it expands to fill the defect completely. It seems to provide a satisfactory method for the operative repair of these communications. When pericardial sacs of proper size were used, closure of the defect was complete and the operation was well tolerated in all the animals but one. In this exceptional case the defect was located close to the myocardial wall in the infundibulum of the right ventricle, and through error the tube was introduced through the right ventricular wall instead of the septum. When the tube was expanded,

it therefore obstructed the pulmonary outflow tract and death resulted. Had the finger been kept within the ventricle during the expansion of the tube, a precaution we now feel should always be taken, its improper placement would have been recognized and it could have been deflated, withdrawn, and replaced.

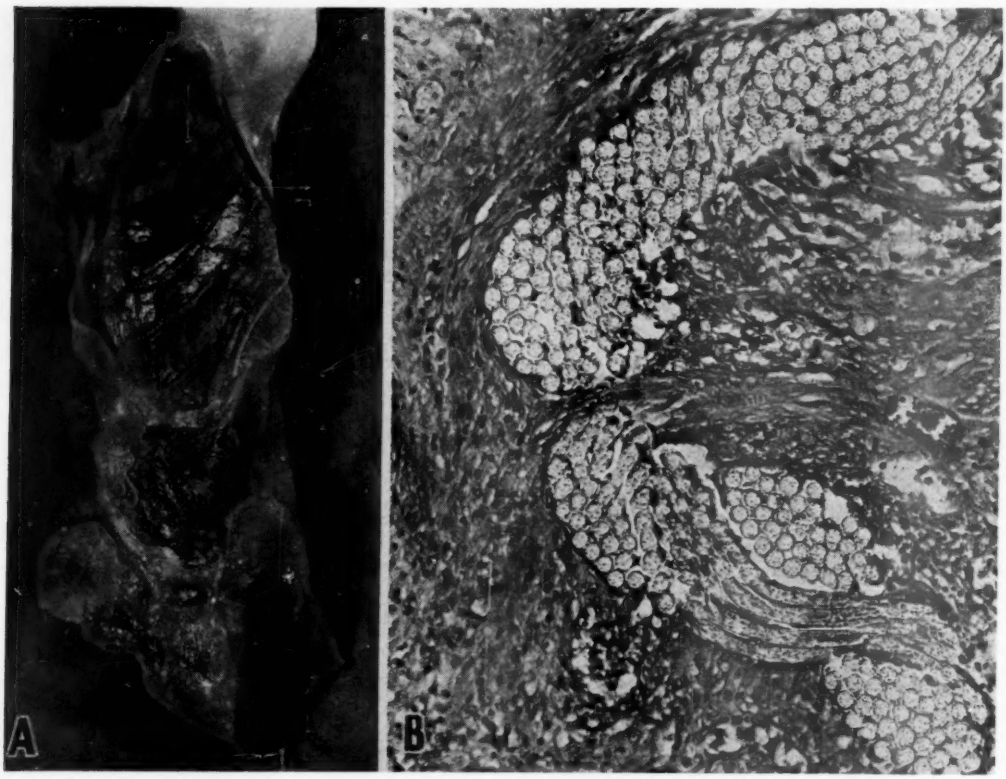

Fig. 11.—Septal defects repaired with nylon grafts, showing (*A*) a vertical section of the septum through the center of the graft one month after repair and (*B*) microscopic evidence of proliferation of fibroblasts and capillaries through the strands of nylon two weeks after repair.

Since the procedure was well tolerated by very ill animals in cardiac failure, it would seem justifiable to conclude that operative repair by this method would be well tolerated by patients. Initial clinical experiences with the operative repair of ventricular septal defects by this method suggest that this is the case.[4] Electrocardiograms made before and after repair in many animals showed no significant abnormalities after closure. The beneficial effect on circulatory dynamics was evident from the moment the defect was repaired. Slowing of the heart rate was often observed immediately and the abnormal pressure relationships within the left and right ventricles reverted toward normal. The color of the lungs usually improved a few minutes later. When closure was complete or nearly complete, animals which were chronically ill from pulmonary congestion and heart failure rapidly became better. If they had been anorexic, a large appetite usually developed on the first postoperative day. A massive ascites which had been present in one dog before repair completely disappeared during the second postoperative week.

It has not yet been determined which material will ultimately prove to be most satisfactory for the construction of the distensible tubes. As far as the experimental animal is concerned, the use of pericardium was entirely satisfactory. The distended graft quickly became adherent to the margins of the defect, and the clot became well organized with fibrous tissue. The question naturally arises as to whether the pericardial graft will survive in human patients, particularly in view of the fact that in one patient in whom a large atrial defect was repaired with pericardium, post-mortem examination of the heart five months afterward showed that the graft had disappeared from the area of the defect.[5] Such an occurrence would seem entirely unlikely, however, when pericardium is used for repair of ventricular defects. These defects in patients are rarely larger than 1 cm. in diameter, and they have a thick septal margin which offers a large surface contact with the graft. In contrast to this situation, atrial defects may be much larger, and viable grafts placed over them must be vascularized from the periphery. It might prove to be a wise precaution in patients, however, to roughen up the margins of the ventricular septal defect and, indeed, to wipe with gauze the mesothelial surface of the pericardium in an effort to promote early adhesion between graft and the margin of defect, and more rapid organization of the thrombus within the graft.

Even though it would appear that pericardial grafts are likely to prove entirely satisfactory for use in patients, it obviously would be wise to study the suitability of other materials in experimental animals. Initial experiences indicate that veins are satisfactory, but it is difficult to obtain an autogenous vein of suitable size. The use of fresh and preserved homologous veins of adequate size should be investigated. Our preliminary observations with the use of nylon suggest that this material may prove satisfactory with the employment of blood as the distending medium. The interstices of the cloth permit the growth of blood vessels and fibroblasts through the tube. It is apparent from our preliminary observations that a thin but much more finely woven cloth than that used would be more satisfactory, since the major difficulty with tubes made of this material resulted from the leakage of blood. Furthermore, the interstices of the sac might be better sealed by a more suitable medium than mineral oil or petroleum jelly. However, even with these deficiencies which were recognized during the course of our experiments, complete closure was obtained in nine of sixteen animals, and almost-complete closure in five, while one of the two real failures was the result of improper placement of the graft itself.

It would be wise, of course, to investigate the possible use of completely impervious materials such as polyethylene or latex for construction of the distensible tube. Up to the present time, the few animals closed with latex have complete closure of the defects, but it is not known whether the latex balloons will be incorporated in a permanent barrier of viable tissue developing from the host. The handmade polyethylene tubes worked well at first and failed because the improvised seal eventually broke and permitted leakage.

Properly constructed tubes of such impervious plastic materials are being obtained and will be studied. If impervious materials are used, the fluid injected for distending them will require further investigation. It is not known whether it would be more satisfactory to use a permanent liquid medium or one which will solidify. It is our plan to investigate a variety of materials both for the construction of the graft and for its distention.

SUMMARY

A seemingly satisfactory method for the operative repair of ventricular defects is described. It involves the passage through the septum and the defect of a tubular graft which, when distended, completely occludes the defect.

Acknowledgment.—We wish to express our deep appreciation to Dr. Frank Vellios for his invaluable assistance in the microscopic observations.

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